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Dissertation

Affect recognition and emotional availability in mother-child interaction: the effect of maternal depression in remission

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Zusammenfassung

Ausgangspunkt der vorliegenden Arbeit ist die gut belegte Assoziation zwischen mütterlicher Depression und ungünstigen emotionalen und behavioralen Folgen für ihre Kinder. Allerdings sind die Faktoren, die zu der transgenerationalen Übertragung der Depression beitragen, noch nicht geklärt. Ziel dieser Arbeit ist es, zwei möglicherweise dazu beitragende psychologische Faktoren zu untersuchen: (1) Affekterkennung von Gesichtsausdrücken in Mutter-Kind Dyaden und (2) mütterliche emotionale Verfügbarkeit. Dazu wurden drei Studien durchgeführt.

Studie I untersucht mittels funktioneller Magnetresonanztomographie (fMRT) unterscheidbare und überlappende Aktivierungsmuster bei gesunden Müttern, während sie fröhliche und traurige Gesichter ihres eigenen Kindes sehen. **Studie II** verwendet eine Morphing-Aufgabe, um die Affekterkennung in Müttern mit remittierter Depression und ihren Kindern zu untersuchen. In **Studie III** wird die emotionale Verfügbarkeit von Müttern mit remittierter Depression in einer Verhaltensbeobachtung untersucht.

Ergebnisse der **Studie I** zeigen eine größere Gehirnaktivierung der Mütter bei traurigen eigenen Kindergesichtern in der Amygdala und anterioren Cingulum, hingegen bei fröhlichen im Hippocampus und inferioren Frontalgyrus. Überlappende Aktivierung wurde in der Insula gefunden. Diese Aktivierungsmuster könnten feinfühliges mütterliches Verhalten erleichtern und das Aufrechterhalten der Mutter-Kind Beziehung unterstützen. Ergebnisse von **Studie II** belegen einen negativen Verarbeitungsbias bei Müttern mit einer remittierten Depression, wobei parallele Veränderungen bei ihren Kindern gefunden wurden. Dies könnte auf einen transgenerationalen Übertragungsprozess hinweisen. Ergebnisse von **Studie III** zeigen eine verminderte emotionale Verfügbarkeit bei Müttern in Remission, was eine Trait-Eigenschaft darstellen könnte.

Schlagwörter: Mutter-Kind Interaktion, emotionale Verfügbarkeit, Affekterkennung, Depression in Remission, transgenerationale Übertragung

Abstract

Starting point of the present dissertation is the well-established association between maternal depression and adverse emotional and behavioral outcomes in children. The factors contributing to the transgenerational transmission of depression have not been fully elucidated. The aim of this thesis is to investigate two psychological factors that potentially contribute to this transgenerational association: (1) affect recognition of facial expressions in mother-child dyads and (2) maternal emotional availability. Therefore, three studies have been conducted.

In **study I**, functional magnetic resonance imaging (fMRI) is used to measure dissociable and overlapping brain activation in healthy mothers, while they view happy, neutral and sad faces of their own child. By using a morphing task, **study II** tests the hypothesis that affect recognition is biased in mothers with depression in remission and their children. **Study III** investigates whether emotional availability is reduced in mothers remitted from depression.

Study I revealed greater brain activation in the amygdala and anterior cingulate cortex while mothers viewed sad faces of their own child, whereas greater brain activation was detected in the hippocampus and inferior frontal gyrus in response to happy faces. Conjoint activation was found in the insula. These activations might facilitate sensitive maternal behavior and promote mothers to maintain the mother-child relationship. Findings of **study II** demonstrate a negative processing bias in mothers with depression in remission, which was paralleled in their children. This finding could possibly point to a process of transgenerational transmission. Results of **study III** indicate reduced emotional availability in mothers who have remitted from depression, which might represent a trait characteristic of depression.

Keywords: mother-child interaction, emotional availability, affect recognition, depression in remission, transgenerational transmission

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1 Introduction

The development of a healthy mother-child relationship depends on sensitive maternal parenting including a mother's ability to respond appropriately to her child's cues – which might be often non-verbal (Knapp, Hall, & Horgan, 2013). It is likely that difficulties in appraising facial expressions of the own child may contribute to a disturbed mother-child relationship and child adversities later in life. Therefore, as a starting point, it is important to understand maternal affect recognition in healthy human functioning.

Acute depression has been identified as one risk factor associated with biased affect recognition (Surguladze et al., 2004) and impaired parenting (Lovejoy, Graczyk, O'Hare, & Neuman, 2000). However, research on mothers with depression in remission is limited. Studying the effects of remitted maternal depression might be especially important in the context of mother-child relationships as the long-term course of depression can be recurrent (Eaton et al., 2008; Steinert, Hofmann, Kruse, & Leichsenring, 2014).

Furthermore, two subtypes of depression have been suggested: with and without history of childhood abuse (Heim, Newport, Mletzko, Miller, & Nemeroff, 2008), which have often not been distinguished in previous research. The questions arise whether mothers with depression in remission show alterations in their affect recognition and in sensitive parenting outside acute episodes and whether maternal history of abuse has an additional impact on these two factors.

In the coming sections, a short summary of the state of the art will be provided, describing relevant findings from research on maternal depression and maternal childhood abuse in relation to parenting behavior, as well as affect recognition. Deducted from this overview, the research questions will be presented. Three studies will then be described that have been designed to address the research questions and thus comprise the empirical part of this dissertation. Finally, in the general discussion, the findings of these three studies will be integrated with previous behavioural and neuroimaging research with emphasis on their novel aspects and potential contributions to future research and clinical practice.

1.1 Affect recognition in healthy mothers

Maternal sensitive behavior probably depends on a mother's ability to respond appropriately to her child's affective states. In the following, this ability is referred to as maternal affect recognition. To appreciate the importance of affect recognition in mothers with history of depression and childhood abuse, one must understand maternal affect recognition in healthy human functioning. At a psychological level, facial affect recognition is fundamental in social development, emotion regulation, and social functioning (e.g., Bistricky, Ingram, & Atchley, 2011; Leppänen & Hietanen, 2001).

Investigations of a neurobiological network that underlies maternal affect recognition have only recently begun (Swain, Lorberbaum, Kose, & Strathearn, 2007). If we better understand the neural basis of maternal affect recognition, we might be able to better understand (and potentially improve) sensitive, as well as neglectful maternal parenting behavior (Swain et al., 2014).

A number of functional magnetic resonance imaging (fMRI) studies have investigated maternal brain responses to images of their child's face (for a review, see Swain, 2008; Swain et al., 2007). Viewing the face of one's own compared to that of another child consistently activated brain areas involved in reward, threat detection, and empathy processes (e.g., ventral striatum, anterior cingulate cortex, hippocampus, inferior frontal/orbito-frontal cortex amygdala, insula) (Bartels & Zeki, 2004; Gobbini & Haxby, 2006; Nitschke et al., 2004; Ranote et al., 2004; Strathearn, Fonagy, Amico, & Montague, 2009; Strathearn & Kim, 2013). These previous studies have focused on maternal responses to facial expressions of infants (0 to 3 years of age). To the best of my knowledge only one small study has previously investigated mothers viewing faces of their primary school-aged (five to 12 years of age) children (Leibenluft, Gobbini, Harrison, & Haxby, 2004). The demands on a healthy mother-child relationship for school-aged children likely change, as children's independence and relationships to other individuals become increasingly important for the child. Thus, maternal responses to their own child's facial expressions might differ depending on the age of the child.

In addition, while these previous studies mainly focused on maternal responses to neutral and happy facial expressions of their own child, studies investigating maternal responses to sad child's faces have only recently begun (Strathearn et al., 2009; Strathearn & Kim, 2013), although responses to sad faces may be at least of the same importance for mother-child

interaction. The question arises, whether maternal responses to sad faces differ from responses to happy faces of the own child.

1.2 Affect recognition and maternal depression

According to mood congruency theories (Beck, 1979), individuals should demonstrate biases only for stimuli that are consistent with their cognitive schemata that underlie their disorder. Therefore, depression should be associated with negatively biased affect recognition, especially for sad facial expressions. A number of studies have investigated alterations in facial affect recognition in depression, consistently indicating a negatively biased processing for sadness: compared to healthy controls, depressed individuals recognized sad faces with higher accuracy (Gollan, Pane, McCloskey, & Coccaro, 2008; Mandal & Bhattacharya, 1985; Sterzer, Hilgenfeldt, Freudenberg, Bermpohl, & Adli, 2011), whereas the opposite has been reported for happy faces (Arteche et al., 2011; Joormann & Gotlib, 2007). Individuals with depression have misinterpreted happy faces as neutral (Leppänen, Milders, Bell, Terriere, & Hietanen, 2004; Surguladze et al., 2004), and ambiguous (Arsenio, Sesin, & Siegel, 2004; Hale, 1998) and neutral facial expressions (Gollan et al., 2008; Gur et al., 1992) as sad. These emotional-cognitive alterations seem to persist during remission (Bhagwagar & Cowen, 2008; Bouhuys, Geerts, & Gordijn, 1999; Fuhr, Hautzinger, & Meyer, 2014; Joormann & Gotlib, 2007; Lange et al., 2012).

The question arises whether biased affect recognition might be transmitted from affected mothers to their children. Investigations addressing this question have only recently begun and suggest that alterations in affect recognition may also exist in children of depressed mothers. The alterations seem mainly to concern sad affects (Joormann, Gilbert, & Gotlib, 2010; Lopez-Duran, Kuhlman, George, & Kovacs, 2013). To the best of my knowledge, to date no studies exist that have directly investigated parallels in affect recognition in mother-child dyads. It remains to be elucidated, whether biased affect recognition in mothers with depression in remission corresponds with respective alterations in their children.

1.3 Affect recognition and maternal childhood abuse associated with psychopathology

The relationship between history of childhood abuse and adult psychopathology has been well established in clinical populations (e.g., Brown & Anderson, 1991) as well as in community samples (e.g., MacMillan et al., 2014). Patients with depression often report a history of childhood abuse, such as physical or sexual abuse (Lizardi et al., 1995; McCabe, Cowen, & Harmer, 2009). Based on neurobiological (Heim et al., 2008; Vythilingam et al., 2002) and treatment studies (Nemeroff et al., 2003), it has been suggested that depressed patients with and without history of abuse represent two distinct subgroups of depression. This distinction may be critical for the investigation of affect recognition (as well as parenting behavior, see section 1.5). In the present dissertation, it was therefore distinguished between mothers with depression in remission with and without history of abuse, i.e. physical or sexual abuse.

In comparison to depressed individuals, fear and anger might be more salient affects for individuals with history of adverse experiences, such as childhood abuse or combat experiences, because they probably are threatening or trauma-related. Research on affect recognition in subjects with posttraumatic stress disorder have primarily relied on functional imaging reporting heightened amygdala activation (Liberzon et al., 1999; Rauch et al., 2000) and reduced medial prefrontal cortex (PFC) activation for fearful facial expressions (Shin et al., 2005); for a review see (Liberzon & Martis, 2006). Similar results have been found for subjects with childhood abuse: amygdala hyperresponsivity to angry facial expressions (Dannlowski et al., 2012) and reduced activation of the medial prefrontal cortex (van Harmelen et al., 2012). The findings probably indicate reduced top-down inhibition of the amygdala by the medial PFC and point to an over-sensitivity of the amygdala to possibly threatening or trauma-related stimuli (Brewin & Holmes, 2003).

Behavioral investigations of affect recognition in individuals with history of adverse experiences are scarce. There was one behavioral study on affect recognition in war veterans (Poljac, Montagne, & de Haan, 2011) indicating biased recognition of sad and fearful facial expressions. To the best of my knowledge, there are no studies, specifically investigating women or mothers with history of childhood abuse and affect recognition. To account for effects of abuse, remitted depressed mothers with and without history of abuse (i.e., physical or sexual abuse) were distinguished in the present dissertation.

Research on affect recognition in depression and history of adverse experiences is characterized by methodological diversity (for a review see Bourke, Douglas, & Porter, 2010): (1) Some studies have used line drawings of facial expressions (e.g., Bouhuys et al., 1999) or static pictures of faces (e.g., Gollan et al., 2008; Surguladze et al., 2004), which might be rather artificial social stimuli. In everyday life, people process a wide range of facial affects, including signals that are less intense than pictures of a standardized set. It is therefore possible that previous studies might not have been ecologically valid enough to capture affect recognition abilities. We addressed this issue by implementing a behavioral affect recognition task where faces are dynamically morphed from neutral to affective. (2) Similarly, the definition of depression has ranged from unipolar depression (e.g., Joormann & Gotlib, 2007) to studies also including bipolar patients (Gur et al., 1992). We therefore clearly defined the index groups as individuals with unipolar depression in remission. (3) At the same time, the definition of history of adverse experiences has varied greatly ranging from emotional abuse and neglect in childhood (e.g., van Harmelen et al., 2012) to firefighter (e.g., Shin et al., 2005) and combat experiences (e.g., Rauch et al., 2000). We defined history of adverse experiences as physical or sexual abuse. (4) In addition, the composition of the control group has ranged from healthy controls without such experiences (e.g., van Harmelen et al., 2012) to healthy ones with the respective experiences (e.g., Poljac et al., 2011). To account for this diversity in the present dissertation, the comparison groups were defined as individuals with unipolar depression in remission with and without history of physical or sexual abuse, compared to healthy controls without history of abuse.

1.4 Parenting behavior and maternal depression

Symptoms of depression, such as loss of joy, sleep disturbances, feelings of blame, and suicidal ideations are likely to prevent depressive mothers to have enough energy and capacity to respond adequately to children's needs (Letourneau et al., 2011). Leckman and colleagues (2009) demonstrated the importance of parenting behavior in the context of maternal depression. In their study, depression proofed to be a significant factor for child behavior problems only if mothers showed poor parenting behavior. Parenting behavior of depressed mothers is often characterized by negative affect (e.g., Field, 1994; Radke-Yarrow & Brown, 1993), impatience (e.g., Tarullo, DeMulder, Ronsaville, Brown, & Radke-Yarrow, 1995),

directive behavior (e.g., Kochanska, Kuczynski, & Maguire, 1989), less responsiveness to children's cues (e.g., Breznitz & Sherman, 1987; Cohn, Campbell, Matias, & Hopkins, 1990), and on the other hand increased controlling and coercive behavior (Dix & Meunier, 2009; Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2003). On the extreme end, these behaviors can activate a cycle of risk transmission. In a meta-analysis by Lovejoy et al. (2000) associations between acute depression and dysfunctional maternal parenting were greatest, however persisting also in mothers with depression in remission. One explanation for persisting effects in mothers with depression in remission are ongoing cognitive vulnerabilities, such as attentional bias (Lange et al., 2012) and mood disturbances (Fava, 1999; Nierenberg et al., 2010). However, research on observed parenting behavior in mothers with depression in remission remains scarce (Breznitz & Sherman, 1987; Lovejoy et al., 2000; Stein et al., 1991; Tarullo, DeMulder, Martinez, & Radke-Yarrow, 1994). It remains to be elucidated whether mothers with depression in remission exhibit impaired parenting behavior.

One research construct that was used in study three to observe the emotional quality of mother-child interactions is emotional availability (Ainsworth, 1978; Biringen, Derscheid, Vliegen, Closson, & Easterbrooks, 2014), which can be described as the affective barometer of a relationship between mother and child (Emde & Easterbrooks, 1985). Mahler and colleagues (1974) have defined emotional availability as a supporting maternal attitude when the child is exploring his environment. Beside physical contact, emotional signalizing and the recognition of such signals are important for emotional availability (Sorce & Emde, 1981), which is addressed as affect recognition in chapter 1.2. and 1.3.. Biringen (Biringen, 2008; Biringen, Robinson, & Emde, 1998) has developed the emotional availability scales where trained raters evaluate the behavior and affect of both, mother and child. Therefore, it takes a dyadic perspective into account where the child is not only the recipient but also contributes to the interaction. There are four adult scales (sensitivity, structuring, non-intrusiveness, and non-hostility) and two child scales (responsiveness and involvement). These scales will be outlined briefly. In addition, a prompt recognition of and responsiveness to child emotional signals are important aspects of maternal sensitivity. Optimal *structuring* would be indicated by setting age-adequate limits to child's behaviour while allowing the child to keep his autonomy. Low scores on *non-intrusiveness* would be given if a mother overly stimulates or interrupts a child's activity and therefore undermine his autonomy. However, the child's reaction is taken into account: If the child enjoys rough playing, this would not be considered as intrusive then. Beside overt *hostility* with words or actions, also covert hostility is rated (signs of anger, impatience, boredom) for this last adult scale. Herewith, maternal hostility

does not have to be directed to the child, but can also address someone else and would still impact on the non-hostility score. On the child's side, signs for non-optimal *responsiveness* are deemed, if the child ignores maternal invitations for interaction or on the other hand if the child is overly responsive and takes every opportunity to keep the contact with the mother (e.g., role reversal). Child *involvement* is considered to be optimal if the child engages the mother into his play, either literally or by making the mother an audience to his play. Again, it is important that the child keeps his autonomy. For a more detailed description of the scales, see Biringen et al. (2014).

Empirical studies demonstrated negative correlations between maternal depressive symptoms and sensitivity (Easterbrooks, Bureau, & Lyons-Ruth, 2012; Lok & McMahon, 2006; van Doesum, Hosman, Riksen-Walraven, & Hoefnagels, 2007), non-intrusiveness (Easterbrooks et al., 2012; Lok & McMahon, 2006; Sorce & Emde, 1981), non-hostility (Easterbrooks et al., 2012; Lok & McMahon, 2006), and structuring (Easterbrooks, Biesecker, & Lyons-Ruth, 2000). Only a few studies have used clinical interviews to assess diagnostic status of maternal depression: depressed mothers were reported to be less sensitive (Trapolini, Ungerer, & McMahon, 2008), less structuring, and more intrusive (Vliegen, Luyten, & Biringen, 2009). However, some studies indicate no differences in emotional availability between depressed and healthy mothers (Fonseca, Silva, & Otta, 2010) and their children (Timmer et al., 2011). One study only found significant differences between healthy controls and a depressed sample with additional psychiatric diagnoses, but not for depression only (Carter, Garrity-Rokous, Chazan-Cohen, Little, & Briggs-Gowan, 2001). In this context, Biringen and colleagues (2014) have pointed to the problem of unpublished null-findings leading to publication biases (Easterbrook, Gopalan, Berlin, & Matthews, 1991; Rosenthal, 1979). It is therefore possible that the association between maternal depression and maternal emotional availability might not be as clear as thought. One aim of the present dissertation is to gain further data to answer this question.

1.5 Parenting behavior and maternal childhood abuse associated with psychopathology

Depressive mothers with concurrent history of childhood abuse might bear an additive or synergetic risk for dysfunctional parenting behavior. Independently of depression, a number of studies have investigated parenting behavior in adults with abusive childhood experiences:

History of sexual or physical childhood abuse has been shown to be a risk factor for poor parenting behavior (Dixon, Hamilton-Giachritsis, & Browne, 2005; Leifer, Kilbane, Jacobsen, & Grossman, 2004; Sidebotham, Golding, & Team, 2001), such as greater use of physical discipline (Banyard, 1997; Bert, Guner, & Lanzi, 2009; Chung et al., 2009; DiLillo & Damashek, 2003; Pears & Capaldi, 2001), and criticism and anger toward the child (Lyons-Ruth & Block, 1996). Others report lower levels of maternal warmth (Barrett, 2010; Pereira et al., 2012) and affect (Lyons-Ruth & Block, 1996).

With respect to maternal history of childhood abuse and emotional availability, studies generally confirm the theoretically-expected inverse relationship between emotional availability and maternal childhood abuse indicating reduced sensitivity (Driscoll & Easterbrooks, 2007; Fuchs, Möhler, Resch, & Kaess, 2015), and increased hostility (Bailey, DeOliveira, Wolfe, Evans, & Hartwick, 2012) and intrusiveness (Moehler, Biringen, & Poustka, 2007), as well as over-responsiveness in children (Timmer et al., 2011).

Despite these extensive findings, the estimates of the rate of intergenerational transmission of childhood abusive experiences varies greatly from 7% (Gil, 1970) to 70% (Egeland, Jacobvitz, & Papatola, 1987). This suggests that, although history of abuse is a risk factor for parents to maltreat their children, parents who do not report abusive childhood experiences might become abusers and many parents who were maltreated as children might not. A number of other variables might contribute to the transmission (e.g., parental psychopathology; see section 1.4.). The high variance may be attributable on the one hand to varying operationalizations of both childhood abuse and parenting and on the other hand to lack of adequate comparison groups (Ertem, Leventhal, & Dobbs, 2000; Kaufman & Zigler, 1987). Furthermore, only a few studies have used behavioral measures of parenting behavior (e.g., Dixon et al., 2005; Lyons-Ruth & Block, 1996).

Only few studies have investigated the impact of maternal childhood abuse on parenting in depressed samples (Ammerman et al., 2012; Cohen, Hien, & Batchelder, 2008; Zalewski, Cyranowski, Cheng, & Swartz, 2013) suggesting an additional effect. To date, such studies relied on questionnaire data for parenting behavior, diagnostic status and childhood abuse. It remains to be elucidated whether maternal childhood abuse additionally impacts on maternal emotional availability in the context of depression.

One aim of the present dissertation is to address the above mentioned methodological limitations by defining maternal history of abuse as sexual or physical abuse, involving

repeated and frequent physical attacks where injuries were likely or sexual contact had happened with a relative, known adult or stranger (Bifulco, Brown, & Harris, 1994). Additionally, it has been proposed that severity of childhood abuse is critical (Newcomb & Locke, 2001). Therefore, mothers with depression in remission with different degrees of childhood abuse were studied. Furthermore, maternal psychopathology and history of abuse were thoroughly assessed using clinical interviews (Bifulco et al., 1994; Hamilton, 1960; Loranger, Janca, & Sartorius, 1997; Sheehan et al., 1998), and maternal emotional availability was observed and evaluated during mother-child interaction (Biringen, Robinson, & Emde, 1998).

2. Research questions

Deducted from this overview of previous research, the present dissertation aimed at addressing the following research questions:

Affect Recognition (study I & study II):

(1) How does brain activation in healthy mothers differ and overlap in response to sad and happy facial expressions of their own child (contrasted to an unfamiliar child)? (study I)
(2) Do mothers with depression in remission exhibit biased affect recognition for sad facial expressions? (study II)
(3) Do affect recognition abilities differ between mothers with depression in remission without history of abuse and remitted mothers with history of abuse? (study II)
(4) Do children of mothers with depression in remission show corresponding alterations in their affect recognition? (study II)

Emotional Availability (study III):

(5) Do mothers with depression in remission show reduced emotional availability in interaction with their children?
(6) Does history of childhood abuse additionally impact on emotional availability among mothers with depression in remission?

3. Summary of studies

To address above mentioned research questions, three studies were conducted at Charité, Berlin, between May 2012 and January 2015 in collaboration with my co-authors as part of the research project "Understanding and Breaking the Intergenerational Cycle of Abuse", which was funded by the German Ministry of Education and Research. In the following three sections, a brief overview of each study will be outlined. For more detailed discussion of the studies, please refer to the manuscripts in the Appendix section.

3.1 Study I: Dissociating neural correlates of maternal parenting behavior in response to happy and sad facial expressions of children in healthy mothers: an fMRI study

The objective of **study I** was to investigate the neurobiological network that underlies maternal affect recognition. A number of fMRI studies have investigated maternal brain responses to images of the own child's face (for a review, see Swain, 2008), however mainly focusing on responses to neutral and happy facial child expressions, although responses to sad faces are presumably of the same importance for the mother-child interaction. The question arises, whether maternal responses to sad differ from responses to happy faces of the own child (research question (1), see section 2. Research questions).

For **study I**, individual visual stimuli were created for each mother, depicting the own and a control child showing neutral, happy, and sad facial expressions, respectively. A total of 30 healthy mothers completed the fMRI task, where they were presented with the individual stimuli and performed an affect recognition task. Overall, the paradigm modulates the factors valence of facial affect (sad (s), neutral (n), happy (h)) and identity (own vs. unfamiliar). Mothers saw 90 pictures of their own child (OC) and 90 of an unfamiliar control child (UC), with 30 pictures for each facial affect, respectively. Pictures were presented in random order for two seconds, followed by a variable inter-trial interval of two to six seconds where a fixation cross was presented. The paradigm consisted of two runs (9 min each). The following contrasts were evaluated for sad valence* identity: 1) ((sad$_{OC}$ > neutral$_{OC}$) > (sad$_{UC}$ > neutral$_{UC}$)), 2) ((sad$_{OC}$>happy$_{OC}$) > (sad$_{UC}$>happy$_{UC}$)). For happy valence *identity: 3) ((happy$_{OC}$ > neutral$_{OC}$) > (happy$_{UC}$ > neutral$_{UC}$)) 4) ((happy$_{OC}$ > sad$_{OC}$) > (happy$_{UC}$ >

sad$_{UC}$)). It was predicted that recognizing the own sad child (OC) compared to an unfamiliar child (UC) would be associated with dissociating and overlapping activations.

Given our *a priori* interest in dissociating and overlapping cortico-limbic regions, region-of-interest (ROI) analyses were conducted for the following regions: ventral striatum, anterior cingulate cortex, hippocampus, inferior frontal/orbito-frontal cortex, amygdala, and insula. For all brain areas, a statistical threshold of $p<0.05$, corrected for multiple comparisons across the whole brain (family-wise error (FWE) rate), was used. The ROI analyses were followed by exploratory whole-brain analyses ($p<.001$, uncorrected) to evaluate the context of the ROI findings. Finally, a conjunction analysis of the two interaction contrasts ((sad$_{OC}$ > neutral$_{OC}$) > (sad$_{UC}$ > neutral$_{UC}$)) and ((happy$_{OC}$ > neutral$_{OC}$) > (happy$_{UC}$ > neutral$_{UC}$)) was conducted to determine common activation profiles of happy and sad faces of one's own child.

Interview measures with sound psychometric properties were used to assess maternal psychopathology (M.I.N.I.; Lecrubier et al., 1997; HAMD; Hamilton, 1960; 1976; IPDE; Loranger et al., 1997) and history of childhood abuse (Childhood Experience of Care and Abuse Interview; CECA; Bifulco et al., 1994; German Translation: Kaess et al., 2011). Maternal history of childhood abuse was defined as physical and sexual abuse, where severe experiences usually involved repeated physical attacks with objects or where injuries were likely or repeated sexual contact with a relative or known adult had happened. For the present study, healthy mothers <u>without</u> history of psychiatric disorders and <u>no</u> childhood abusive experiences were recruited.

Findings of **study I** confirmed our hypotheses: In particular, viewing the own child with sad facial expressions activated the amygdala, anterior cingulate cortex, insula, and hippocampus, which may be considered areas of a threat detection network. In contrast, viewing the own happy child activated the (para)hippocampus, insula, precuneus, and inferior frontal gyrus, i.e., areas that may be regarded part of a reward network. Overlapping areas for sad and happy faces of the own child included the insula and superior temporal gyrus, which may relate to an empathy network. It may be speculated that these differential responses may facilitate fast and adequate reactions of the mothers, e.g., vigilant protective behavior in response to sad child faces and sensitive parenting behavior in response to happy, rewarding child faces. One might presume that this activation pattern might be reduced or diminished in mothers with remitted depression or childhood abusive experiences.

3.2 Study II: Transgenerational effects of maternal depression on affect recognition

In study I, we were interested in the neurobiological network that underlies affect recognition in healthy mothers. The objectives of **study II** were to investigate on a behavioral level whether affect recognition was altered in mothers with depression in remission, either with or without history of abuse, and whether these alterations are transmitted to their children (research questions (2) to (4), see section 2. Research questions). Given that the development of a healthy mother-child relationship depends on a mother's ability to respond adequately to her infants' cues and that the processing of facial expressions is an essential feature in human interaction, it is likely that difficulties in recognizing facial expressions may contribute to the problematic interactions between mothers with history of depression and abuse and their children (see study III).

In total, 81 mother-child dyads completed an affect recognition task where facial expressions of adult faces morphed gradually and continuously from neutral to happy, sad, angry, or fearful (see Figure 1 for an example). Mothers completed 64 trials (16 trials for each affect). They were asked to press a stop button as soon as the recognized the emerging affect and then selected one of them by forced choice. Children performed the same task with two modifications: the affect category of fear was excluded and only 36 trials were implemented. Children were also asked to press a stop button, but depending on their age, they could select the affect category either by button press or verbally. Three outcome variables were analyzed: 1) response times, 2) accuracy score, and 3) response bias in incorrect trials. At group level, repeated-measures analyses of variance (ANOVA) were conducted. At dyadic level, two-tailed Pearson's correlations were implemented. The same diagnostic measures were applied as in study I. Maternal history of abuse was defined as either childhood or adulthood physical or sexual abuse.

Figure 1: Example for the affect of anger

Mothers with depression in remission showed an increased accuracy for sad facial expressions, as well as a sadness bias. Strikingly, their children's affect recognition abilities were very similar, with an increased sadness bias. At dyadic level, maternal and children's accuracy and bias scores for sadness were positively correlated, the latter, however, only at trend-level. There were no differences between remitted groups with and without history of abuse.

Our data suggest that mothers with depression in remission have a processing bias for sad facial expressions which may contribute to recurrent depressive episodes. This finding also implies that children are exposed to their mother's processing bias not only during acute depression but also during remission. Strikingly, children's affect recognition was found to be similarly biased and to be correlated with their mother's affect recognition, which possibly implies a transgenerational transmission process. In children, this processing bias may contribute to behavioural and emotional problems.

3.3 Study III: Emotional Availability in mother-child dyads: the impact of maternal depression in remission and additional maternal childhood abuse

Maternal depression and history of childhood abuse have independently been associated with diminished parenting behavior (e.g., Lovejoy et al., 2000; Widom, 1989). However, individuals with childhood abuse often develop a psychiatric disorder, such as depression. There are a few studies investigating the impact of maternal childhood abusive experiences on parenting in depressed samples, though relying on questionnaire data solely (Ammerman et al., 2012; Cohen et al., 2008; Zalewski et al., 2013). Research on observed parenting behavior in remitted depressed samples is scarce (Lovejoy et al., 2000). **Study III** therefore aimed at addressing research questions (5) and (6) (see section 2. Research questions).

In total, 188 mother-child dyads (N=89 healthy controls, N=89 mothers with depression in remission) were observed while playing together in a standardized playroom setting: for the first 15 minutes dyads were asked to play as they usually would. For an additional 6 minutes, children were asked to solve a puzzle task with the help of their mothers. The quality of the mother-child interaction was rated by means of the Emotional Availability Scales (EAS, 4th Edition, Biringen, 2008), which comprise four adult scales (emotional sensitivity, structuring,

non-intrusiveness, non-hostility). The EAS allow one to rate the emotional quality of mother-child relationship and is considered to be a dyadic construct, meaning high scores on the adult scales can only be achieved if the child is appropriately responsive and involving. Three coders were trained by Zeynep Biringen and blinded to maternal history of depression and childhood abuse. Interrater reliability for pairs of raters ranged between r=.78 and r=.86 for "sensitivity", between r=.81 and r=.87 for "structuring", between r=.82 and r=.86 for "non-intrusiveness", and between r=.84 and r=.90 for "non-hostility" (average-measure intra-class correlations), indicating excellent agreement (Cicchetti, 1994). The same diagnostic measures were applied as in study I.

To test, whether depression in remission impacts on maternal emotional availability, univariate analyses of covariance (ANCOVA) with history of depression as between-subject factor were calculated. As groups differed regarding partnership status and Hamilton depression scores, these variables were taken as covariates into account in the analyses. In addition, childhood abuse was controlled for by including the CECA sum score of its main scales (neglect, parental antipathy, psychological, physical and sexual abuse). In a second analysis step, ANCOVAs were run to evaluate the effect of additional history of childhood abuse on emotional availability among mothers with depression in remission. For this analysis, the remitted depression group was subdivided according to their degree of childhood abuse in three groups: a) without, b) with mild to moderate, c) with severe history of childhood abuse.

Interestingly, remitted depression had an effect on emotional availability reducing maternal sensitivity (even after applying Bonferroni correction), structuring, and non-hostility. This finding possibly indicates that children may be exposed to their mother's reduced emotional availability not only during acute depressive episodes but also during remission. In the second analyses on the impact of various degrees of maternal childhood abuse among mothers with depression in remission, mothers with severe history of childhood abuse were significantly less sensitive than remitted mothers without childhood abuse. At trend-level, similar results were found for maternal hostility. The impairments reported here may represent a trait characteristic of depression. It is obvious that persistent alterations of parenting behavior will have greater impact on the children's development and well-being, e.g., it may affect the child's intellectual development (Hay et al., 2001) and add to emotional and behavioral problems (Cox, Puckering, Pound, & Mills, 1987). Our data suggest an additional effect of maternal childhood abuse on emotional availability in mothers with depression in remission in

case of severe childhood abusive experiences. The absence of an additional effect of mild to moderate childhood abuse might be due to the sample size. An alternative explanation is that, in these cases, the history of depression may be the determining factor, overriding effects of mild to moderate childhood abuse.

The results of **study III** may help to explain the well-established unfortunate finding of increased emotional and behavioral problems in children of parents with depression. Especially experiences of severe maternal childhood abuse might further impact on the mother-child interaction among mothers with depression in remission.

4. General discussion

In summary, our findings indicate that on the neuronal level of affect recognition, healthy mothers showed dissociable activations to sad and happy facial expressions (research question 1) that possibly links to maternal sensitivity: recognizing the own sad child compared to an unfamiliar child was associated with activation in areas involved in threat detection (amygdala, anterior cingulate cortex, insula, and hippocampus), whereas recognizing the own happy child compared to an unfamiliar child was associated with activation in areas involved in reward ((para)hippocampus, insula, precuneus, and inferior frontal gyrus). Conjoint activation was found in areas related to empathy (insula and superior temporal gyrus). On the behavioral level, remitted depressed mothers exhibited altered recognition of sad facial expressions (research question 2). However, affect recognition abilities did not significantly differ between remitted mothers with and without history of abuse (research question 3). Furthermore, maternal affect recognition resembled the one in their children (research question 4), maybe showing a path of transgenerational risk transmission and posing the children at elevated risk for developing affective disorders as well. In mother-child interaction, remitted depressed mothers showed reduced emotional availability (research question 5). In particular, they were less sensitive and, at trend-level, more hostile and less structuring toward their children. In other words, children of remitted depressed mothers seem to be exposed to biased affect recognition and reduced maternal sensitivity even outside acute maternal depressive episodes. Among mothers with depression in remission, our results show an additional effect of severe history of childhood abuse for maternal sensitivity (research question 6).

4.1 Neural basis of affect recognition in mothers

In **study I** of the present dissertation, the neural basis of affect recognition was studied in healthy mothers in response to happy and sad facial expressions of their own child compared to an unfamiliar child. Our findings implicate that maternal brain responses differ depending on their child's affective state.

Most previous studies on maternal perception of the own child's face have relied on neutral and happy facial expressions (Bartels & Zeki, 2004; Nitschke et al., 2004; Ranote et al., 2004) and found activation in the orbitofrontal cortex, striatum, thalamus, and hypothalamus. Going one step further, in **study I**, we also studied maternal responses to sad child faces and found activation in the amygdala, anterior cingulate cortex, insula, and hippocampus which have been associated with a variety of processes, including fear processing (LeDoux, 2003), salience detection (Ousdal, Reckless, Server, Andreassen, & Jensen, 2012), and empathizing with the pain of a loved one (Singer et al., 2004). One may tentatively suggest that recognizing the own child's sad face activates a threat detection network in the mother (Britton et al., 2006; Phelps et al., 2001; Swain et al., 2007).

While sad faces produced activations in the amygdala and ACC, happy faces (own versus unfamiliar child) produced activation in the inferior frontal gyrus, precuneus, and (para)hippocampus. These latter regions have been associated with reward processing (Albrecht, Volz, Sutter, & von Cramon, 2013; Swain, 2008) as well as the retrieval of person knowledge and episodic memories (Burgess, Maguire, & O'Keefe, 2002; Gorno-Tempini et al., 1998; Leveroni et al., 2000).

From an evolutionary perspective, it is likely that specific brain mechanisms in mothers have developed to secure the survival of their offspring. Different stages of processing may be distinguished in maternal responses to their child's affective states, starting from early (subcortical) visual information processing through more complex (cortical/prefrontal) perceptive processes to motor actions. At the same time, it is obvious that adequate maternal responses to sad and happy affective states will differ. Our data from the affect recognition task (requiring perception but not motor action) indicate that this difference is already present during perceptive stages of the maternal responses, even during early subcortical visual information processing. It may be speculated that these early differential responses to sad and happy faces may facilitate fast and adequate reactions of the mothers, e.g., vigilant protective

behavior in response to sad child faces and sensitive parenting behavior in response to happy, rewarding child faces.

In addition to dissociable networks, our paradigm also allowed us to identify brain areas showing overlapping activations to both happy and sad facial expressions of the own child. We found activation in areas associated with cognitive and affective aspects of empathy, such as the superior temporal gyrus and the insular regions (Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Chakrabarti, Bullmore, & Baron-Cohen, 2006; Gallagher & Frith, 2003; Gobbini & Haxby, 2006; for a meta-analysis, see Fan, Duncan, de Greck, & Northoff, 2011). The common network possibly reflects healthy mothers' ability to understand their child's intentions and wishes, and to react sensitively to them.

In **study I**, static photographs of one's own child and an unfamiliar control child were used, which is already an advantage over pictures of standardized sets. Future research should aim to explain affect recognition and neural basis of maternal sensitivity by approaching real conditions of social communications (e.g., video-clips of one's own mother-child interaction), and taking the context of situations into account. New technological developments should help to create even more realistic and complex multimodal stimuli, including various perceptual domains (e.g., visual, auditory, and tactile), and the social context (e.g., conversational context) in which stimuli usually appear.

What do these findings in healthy individuals imply for mothers with history of depression which we have studied in **study II** and **III**? Hyper-activation in parts of an evolutionarily important threat-detection system like the amygdala could contribute to the development and maintenance of depressive episodes. One might tentatively suggest that the results of **study II** point toward a hyper-activated threat-detection system at the behavioral level: mothers with depression in remission showed greater accuracy for sadness, as well as a greater response bias during trials where other affects were misinterpreted as sad. Since the processing of facial expressions is fundamental for social interaction, an altered threat detection system could be one sign of the frequently observed interpersonal problems, including social withdrawal, and feelings of interpersonal rejection (Stuhrmann, Suslow, & Dannlowski, 2011). This could hinder a depressed mother to react sensitively in stressful emotional situations, such as coping with a crying child. In line with this assumption, in **study III**, mothers with depression in remission were found to be less sensitive during mother-child interaction.

4.2 Impact of depression in remission

Even though mothers were currently euthymic, remitted depression was shown to impact on maternal affect recognition (**study II**) and parenting behavior (**study III**) toward the child. This could imply that 'it's not over, when it's over' as it has also been suggested for neurobiological alterations in individuals with depression in remission (Bhagwagar & Cowen, 2008). From a clinical point of view, these results are rather disillusioning as over 80% of the mothers with depression in remission had received psychotherapy in our sample so that one might have hoped to find mothers with remitted depression to resemble healthy control mothers.

Our results are meaningful as one must not forget the children who seem to be exposed to altered affect recognition and reduced emotional availability of their mothers even in phases of remission. The mean time elapsed since last depressive episode and the current study appointment was 61.6 months (ranging between two and 330 months). Children of these studies were required to be between five and 12 years old (approx. between 60 and 144 months). It is therefore possible that the maternal episode of depression occurred before the child's lifetime, at least for some of the dyads. Therefore, children might be influenced by their mothers' remitted depression, even though it has occurred before the child's lifetime. However, a separate analysis with maternal depression during and outside children's lifetime as additional factor would be necessary to confirm this assumption.

Children of both depression groups (i.e., with and without history of abuse) showed a response bias for sadness, similar to their mothers. To the best of my knowledge, study II is the first to show corresponding alterations between remitted mothers and their children. The negative processing bias in maternal affect recognition might influence the child's affect recognition abilities as the mother is usually the most important model from which the child learns emotional and social skills during the first years of childhood (Goodman & Gotlib, 1999). Children might have acquired biased affect recognition through social learning in form of modeling processes. Accordingly, children have been found to mirror negative cognitions of their depressed mothers, such as being more self-critical and having lower self-concepts (Downey & Coyne, 1990), and, as we have found in **study III**, children of mothers with history of depression are exposed to reduced maternal emotional availability. Our corresponding findings in children's affect recognition **(study II)** might reflect modeling of maternal negative thinking, or the experience of having been frequently reinforced to hold

negative views about the world or oneself. This negative processing bias in children might place them at elevated risk for experiencing depressotypic feelings and thoughts similar to the ones exhibited by their mothers. This could make them more vulnerable to developing affective disorders themselves (Goodman et al., 2011).

Beside cognitive processes, one likely biological mediator might be the neuropeptide oxytocin which has been linked to affect recognition performance in healthy adults (Van Ijzendoorn & Bakermans-Kranenburg, 2012) and appears to be reduced in depressed mothers (Apter-Levy, Feldman, Vakart, Ebstein, & Feldman, 2014), as well as in individuals with history of childhood abuse (Heim et al., 2009). In future studies, biological mediators and moderators should be taken into account.

Traditionally, research on behavioral and cognitive alterations in depression has focused on abnormalities associated with the acute episode which could represent a state marker. Investigating individuals recovered from depression might allow one to study possible trait markers of vulnerability (Bhagwagar & Cowen, 2008), such as affect recognition. From a methodological point of view, however, this kind of research leaves one uncertain whether altered affect recognition was present before the onset of the depression and contributed to its onset (i.e., constituting a vulnerability factor), or instead, is a "scar" of the depression (Rohde, Lewinsohn, Klein, & Seeley, 2005) that in turn may also increase the vulnerability of recurrence of depression. Disentangling the state-trait question would be important also for a better understanding of the impact of maternal depression on child well-being. It could be that maternal trait markers have a long-lasting effect on children that could already be mitigated prior to the onset of maternal depression or child psychopathology. Screening for and targeting maternal and child symptoms that may not yet be impairing might be one consideration for preventive interventions and treatments (see section 4.4. Implications for treatment). Unfortunately, in the case of our findings for both affect recognition and emotional availability, we do not have data on affect recognition skills and parenting qualities prior to the onset of maternal depression. For future studies, a way out might be implementing a cognitive or behavioral "high-risk paradigm" (Just, Abramson, & Alloy, 2001) where never-depressed participants are recruited who show high or low levels of biased affect recognition (e.g., sadness bias) or of emotional availability as presumed vulnerability factor for depression. These high and low risk groups would then be followed up on their likelihood to develop a depression in the future.

4.3 Impact of history of additional abuse

It is well-established that history of childhood abuse increases the risk for developing major depression in adulthood (Bifulco, Brown, & Adler, 1991; Chapman et al., 2004). Furthermore it has been suggested that there might exist two subtypes of depression, with and without history of abuse (Heim et al., 2008). In theory, effects of remitted depression and history of abuse could add up. Alternatively, it is also possible that the effect of maternal psychopathology is more pronounced and overrides the effect of history of abuse. The aim was therefore to investigate whether concurrent history of abuse additionally impacts on affect recognition and emotional availability among mothers with depression in remission.
For emotional availability (**study III**), an additional effect of history of physical or sexual childhood abuse was found in case of severe abuse, such as being raped or ongoing physical abuse in childhood with life threatening or severe injuries. Mothers with depression in remission and severe history of childhood abuse were less sensitive compared to remitted mothers without any history of childhood abuse. These findings are in accordance with Heim's and her colleagues' (Heim et al., 2008; Heim et al., 2009) theory of two subtypes of depression. For affect recognition (**study II**), however, there were no differences between mothers with remitted depression with and without history of abuse. This could have at least two reasons:

(1) Affect recognition could be considered as a primarily cognitive task, where cognitive processes like perceptual processing and retrieval of emotion knowledge are necessary (Adolphs, 2002). In contrast, maternal sensitivity might require mainly interactive and affective skills. This is reflected in the definition of maternal sensitivity (Biringen et al., 2014), where a positive and authentic affective climate between mother and child is necessary to receive high scores. It is therefore possible that mothers with depression in remission and history of abuse do not show additional cognitive impairments, but that history of abuse impacts on affective components of maternal behavior.

(2) A second explanation for these results could be that the emotional availability scales are more sensitive in identifying differences between mothers with depression in remission with and without history of abuse than a morphing task. Raters of maternal sensitivity were blinded and highly trained to recognize even subtle forms of insensitivity (e.g., apparent/unreal affect quality). The affect recognition task relied on maternal response times and accuracy rates

which might not be sensitive enough to capture differences between mothers with depression in remission with and without history of abuse.

In future studies on affect recognition and emotional availability, it would be interesting to investigate the effect of various aspects of abuse, such as duration and frequency of abuse, age at onset of abuse, relationship of perpetrator, comorbid adversities such as financial difficulties at home, and parental discord, as well as social support, and coping mechanisms. Beside physical and sexual abuse, also other types of abuse like emotional abuse and neglect should be taken into account (DiLillo & Damashek, 2003). A greater knowledge on the impact of these factors would also help to find resilience factors that can be strengthened in treatment (Collishaw et al., 2007; Taylor & Harvey, 2010; Wright, Fopma-Loy, & Fischer, 2005). In line with this, it would be desirable to have a second healthy control group with history of abuse. This would allow one to separate the effect of depression and abuse. This was beyond the scope of the present dissertation, however the research group has recruited a group of healthy controls resilient to their history of childhood abuse by now and will address above mentioned issues.

4.4 Implications for treatment

Based on the findings of the present dissertation mothers with depression in remission and their children might benefit from interventions that improve maternal sensitivity and target biased affect recognition. Especially time of remission might be a critical period for mothers to train and improve their parenting qualities and alterations in affect recognition. Our results in remission (**study II & III**) may motivate mothers to actively seek treatment. In the following section, two kinds of treatments that might be helpful to target the alterations that we have observed in affect recognition and maternal sensitivity will be discussed.

Parent-Child Interaction Therapy (PCIT; Eyberg & Robinson, 1982) is a manualized parent training over 12 sessions that has been identified as an evidence-based treatment of disruptive behavior of children (for a review see Gallagher, 2003; Thomas & Zimmer-Gembeck, 2012). It is designed to directly improve the parent-child relationship by live-coaching parents during their interaction with their child. In fact, several studies have reported that maternal and child emotional availability scores had improved after PCIT (Dombrowski, Timmer, Blacker, &

Urquiza, 2005; Timmer et al., 2011). Though this behavioral training has much to recommend it (e.g., immediate feedback possible by live-coaching, rehearsing acquired new skills weekly during interaction with their child, manualized training), the attrition rates usually range between 27 to 47% (Bagner & Eyberg, 2007; Berkovits, O'Brien, Carter, & Eyberg, 2010; Boggs et al., 2005). Some studies have reported percentages as high as 66% (Lyon & Budd, 2010) or even 77% (McNeil, 2007). This lets one assume that if treatment barriers are reduced, this kind of treatment might be effective in improving maternal sensitivity which we have found to be reduced in mothers with depression in remission.

An alternative treatment approach to the rather behaviorally driven PCIT might be the concept of mindful parenting which has lately received considerable attention in the literature (Bögels, Lehtonen, & Restifo, 2010; Cohen & Semple, 2010; Duncan, Coatsworth, & Greenberg, 2009). This kind of treatment might help targeting both, biased affect recognition and emotional availability, which we have found to be altered in mothers with depression in remission (**study II & study III**). One proposed dimension of mindful parenting is 'listening with full attention' (Duncan et al., 2009) which might be related to affect recognition abilities. Mindful parents might direct their full attention to their child that goes beyond simply hearing what the child says, and also takes the child's facial expressions, and body language into account to detect their child's needs or intended meaning. This could help to reduce the sadness bias that we have found in mothers with depression in remission. Applying "compassionate attention" (Duncan et al., 2009) may also counteract the negative processing bias that we have found by letting the parent deliberately attend to caring feelings towards herself and the child. Furthermore, adopting a 'non-judgmental, accepting' and 'compassionate' stance toward oneself (Bögels et al., 2010; Duncan et al., 2009) might be a prerequisite for healthy parenting and therefore improve also maternal emotional availability. If mindfulness-based parenting programmes are offered to mothers with depression in remission this could prove beneficial to both, mother and child.

5. Conclusion

The present dissertation investigated two psychological factors that potentially contribute to the transgenerational association between maternal depression and adverse outcomes in children: (1) affect recognition on the neuronal (study I) and behavioral level (study II), and (2) maternal emotional availability in mother-child interaction (study III).

Our results in healthy mothers suggest that dissociable brain responses to sad and happy facial expressions of the own child can already be observed during perceptive stages of the maternal responses, i.e., during early subcortical visual information processing **(study I)**. These differences might facilitate sensitive maternal behavior and promote mothers to maintain the mother-child relationship. Altered activation of these neural networks might negatively impact on parenting behavior. This has to be shown in future studies including mother-child dyads showing dysfunctional interaction. Our behavioural results (study II & III) in mothers with depression in remission support the conclusions drawn from the neuronal level: during remission, mothers with depression showed (1) biased affect recognition (**study II**), particularly concerning sad facial expressions. This persistent processing bias might impact through mother-child interaction also on the offspring. We found striking parallels between mothers and children both at group and at dyadic level. Our findings could possibly point to a transgenerational transmission process. In the next generation, this bias may again increase the risk for developing depressive symptoms, as in the mothers. (2) Reduced emotional availability (**study III**), particularly maternal sensitivity. This finding appears to be relevant for both mothers and children, as such persistent alterations may contribute to continuing social interaction problems in mothers and through social learning also impact on the offspring. In addition, our results in remitted mothers suggest an additional effect of severe childhood abuse on maternal sensitivity.

Practicing mindful parenting and particularly being mindful during emotionally intense, and stressful parent-child interaction could prevent and stop transgenerational transmission of dysfunctional parenting and risk for child psychopathology.

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7. Appendix

7.1 Original manuscripts

7.1.1 Study I

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Title: Dissociating maternal responses to sad and happy facial expressions of their own child: an fMRI study

Short title: maternal responses to sad and happy faces of their own child

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Abstract

Background:

Maternal sensitive behavior depends on recognizing one's own child's affective states. Previous research has mainly focused on maternal response to neutral and happy child facial expressions. The present study investigated distinct and overlapping neural responses of mothers to sad and happy facial expressions of their own child.

Methods:

We used functional MRI to measure dissociable and overlapping activation patterns in 27 healthy mothers, while they viewed happy, neutral and sad facial expressions of their own school-aged child and a matched unfamiliar child. During the scan, mothers were asked to press a button indicating the affect of the presented face. After scanning, they were asked to rate the perceived emotional arousal and valence levels for each face using a Likert-scale.

Results:

While viewing their own child's sad faces, mothers showed activation in the amygdala and anterior cingulate cortex. Viewing one′s own child's happy facial expressions elicited activation in the hippocampus and inferior frontal gyrus. Conjoint activation was found in the insula and the superior temporal gyrus.

Conclusions:

Maternal brain activations differed depending on the child's affective state. Sad faces of the own child activated a threat detection network in the mother, whereas happy faces activated brain reward regions. Overlapping activation was found in empathy related networks. These differences might facilitate sensitive maternal behavior.

Introduction

The mother-child relationship is fundamental for the child to learn emotional and social skills during the first years of childhood. Sensitive maternal behavior has been argued to be essential for the normal development and mental health of a child [1, 2]. The quality of sensitive behavior depends on a mother's ability to respond to her child's cues, such as appraising her child's facial expressions. In the following, we will refer to this ability as maternal affect recognition. Investigations of a neurobiological network that underlies maternal affect recognition have only recently begun. A better understanding of the neural basis of maternal affect recognition might help to better understand (and potentially improve) sensitive, as well as neglectful maternal parenting behavior [3].

A number of fMRI studies have investigated maternal brain responses to images of their child's face (for a review [4, 5]). Viewing the face of one's own compared to that of another child consistently activated brain areas involved in reward, threat detection, and empathy processes (e.g., ventral striatum, anterior cingulate cortex, hippocampus, inferior frontal/orbito-frontal cortex, amygdala, insula) [6-10]. While these previous studies mainly focused on maternal responses to neutral and happy facial expressions of their own child, studies investigating maternal responses to sad child's faces have only recently begun [9, 10], although responses to sad faces may be at least of the same importance for mother-child interaction. The question arises, whether maternal responses to sad differ from responses to happy faces of their own child.

In addition, previous studies have focused on maternal responses to facial expressions of infants (0 to 3 years of age). To the best of our knowledge only one small study has previously investigated mothers viewing faces of their school-aged (five to 12 years of age) children [11]. The demands on a healthy mother-child relationship for school-aged children presumably change, as their independence and relationships to other individuals become increasingly important. Thus, maternal responses to their own child's facial expressions might differ depending on the age of the child.

In the present study of healthy mothers, we created individual picture stimuli for each mother, depicting the own and a control child with neutral, happy, and sad facial expressions, respectively. Children were between five and 12 years old. During fMRI, mothers were presented with the individual pictures and performed an affect recognition task on the facial expressions. This allowed identifying dissociable and overlapping neural responses of mothers to happy and sad facial expressions of their own child (compared to an unfamiliar child).

We predicted that recognizing one's own sad child (OC) compared to an unfamiliar child (UC) would be associated with dissociating and overlapping activations in brain areas implicated in emotion processing and social cognition.

Methods and Materials

Subjects

Thirty healthy subjects were recruited by advertisement. Subjects were right-handed women between 27 to 48 years of age (mean: 39.5 ±5.5) whose (nonadopted) healthy child was between five and 12 years old (mean: 7.8 ±1.6; 43% girls). Handedness was assessed using the Edinburgh Handedness Inventory [12]. The absence of psychiatric illness was confirmed by a structured psychiatric diagnostic interview for axis-I disorders (M.I.N.I; Mini international neuropsychiatric interview [13]) and axis-II disorders (for the following three personality disorders: emotional-instable, unsecure, antisocial; International Personality Disorder Examination [14]). The study was approved by the ethics committee of the Charité - Universitätsmedizin, Berlin. The present study was performed within the framework of the project UBICA ("Understanding and Breaking the Intergenerational Cycle of Abuse"). Findings from the clinical samples of the UBICA study will be reported elsewhere. We here focus on findings from healthy subjects recruited at the Berlin study site. All subjects gave written informed consent before participating. Subjects were reimbursed for their participation. Data of three subjects were excluded from analyses because of excessive head movement (exclusion criterion > 2 mm and/or 2° within one run), leaving twenty-seven subjects for final analyses.

Pictures

In preparation for the fMRI experiment, individual picture stimuli were created for each mother which depicted sad, happy, and neutral facial expressions of her child. These pictures were obtained during a mood induction session with a trained study assistant: As most sessions took part in the afternoon after school, a mindfulness exercise was performed first, to make children more aware of their external surrounding as well as their internal body sensations. Children were then asked to remember a sad situation they had experienced recently. They were asked to look, walk and behave as if they were sad again. Thereafter, children watched short sad video clips of movies (e.g., "The Lion King" by Disney) while their facial expressions were videotaped. Happy expressions were obtained while children watched comic movies (e.g., "Mickey Mouse" by Disney). Neutral expressions were obtained prior to mood induction. A team of three study associates rated all facial pictures with respect to the shown valence on a 7-point Likert-scale ranging from very sad (-3) to very happy (+3). Pictures were selected if the rater team agreed upon the valence. Only pictures with moderate valence (i.e., a score of +2 for happy and a score of -2 for sad) and neutral pictures (i.e., a score of 0) were selected for the experiment ensuring a perfect match between the own and unfamiliar child. In all pictures, the children faced the camera straight on. Pictures

were digitized and cropped to show only the faces. Age- and gender-matched pictures of six unfamiliar children were used as control pictures (unfamiliar child, UC).

Task

During fMRI, the pictures of the own and a control child were presented to the mother who performed an affect recognition task. While viewing the pictures, the mothers was asked to indicate via button press for each facial expression as soon and as accurately as possible whether it was sad, happy, or neutral. Overall, the paradigm modulates the factors valence of facial affect (sad, neutral, happy) and identity (own vs. unfamiliar). Mothers saw 90 pictures of their own child (OC) and 90 of an unfamiliar control child (UC), with 30 pictures for each facial affect, respectively. Pictures were presented in random order for two seconds, followed by a variable inter-trial interval of two to six seconds where a fixation cross was presented. The paradigm consisted of two runs (9 min each). Pictures were presented to the mother on an overhead mirror display. Before entering the scanner, subjects performed a training session to get familiarized with the task. After scanning, pictures were presented to the subjects for a second time and subjects were asked to rate each picture with regard to valence and arousal [15].

Imaging

MRI data were acquired using a 3 T whole-body MRI scanner (MAGNETOM Trio, TIM-Technology; Siemens, Erlangen, Germany) with 32-channel head coil and a standard T2-weighted echo planar imaging (EPI) sequence, sequential descending acquisition, flip angle $\alpha=78°$, 64x64 pixels in-plane resolution, 33 slices, voxel dimensions 3x3x3 mm^3, a 0.75-mm gap between slides, field of view 192x192 mm^2. For each run, 257 scans were acquired whereas the first six images of each run were discarded to account for possibly incomplete signal saturation. After the functional session, a T1-weighted high-resolution structural scan was obtained to detect potential abnormalities (none was detected).

Statistics

Behavioral data

Response times, hit rates (i.e., percentage of correct answers for each condition), post-scan valence and arousal ratings for the six conditions were compared using separate repeated-measures analyses of variance (ANOVA) with valence of child affect (sad, happy, neutral) and identity (own vs. unfamiliar) as within-subject factors. Degrees of freedom were Greenhouse-Geisser corrected whenever necessary [16, 17]. For clarity, the uncorrected degrees of freedom are reported. Significance was set at $p<0.05$. Post hoc analyses were performed using paired t-tests with Bonferroni correction for multiple comparisons

(p=0.05/3=0.017). Response times and hit rates are missing for one subject due to technical problems. All behavioral data analyses were carried out using SPSS 18 (IBM; Armonk, NY, USA). Association between mothers' self-reported arousal and valence ratings for one's own child and peak activation of BOLD responses in predetermined ROIs (see below) were examined in correlational analyses.

fMRI Analysis

Data analysis was performed with Statistical Parametric Mapping 8 (SPM 8, Wellcome Department of Cognitive Neurology, London, UK) running on MATLAB (Mathworks Inc, Sherborn, MA, USA), with the following preprocessing procedure: slice-time correction and spatial realignment, normalization to the standard Montreal Neurological Institute (MNI) echo-planar imaging (EPI) template using third-degree B-spline interpolation and spatial smoothing with an 8-mm full width at half maximum isotropic Gaussian kernel. Statistical analysis was carried out using the first-level general linear model (GLM) function in SPM. For each subject, six stimulus types (own and unfamiliar faces with neutral, happy, or sad expressions, respectively) were used as regressors. Hemodynamic responses to each stimulus were modeled with a delta function convolved with a synthetic hemodynamic response function. Low-frequency noise was removed by applying a highpass filter (cut-off: 128 s) to the fMRI time-series at each voxel. Linear contrasts for each experimental condition were created by averaging the same experimental conditions across the two runs. These individual contrasts were submitted to the group level using a second-level full-factorial analysis. The following interaction contrasts were evaluated for <u>sad valence</u> * identity:

1) $((sad_{OC} > neutral_{OC}) > (sad_{UC} > neutral_{UC}))$

2) $((sad_{OC} > happy_{OC}) > (sad_{UC} > happy_{UC}))$.

The following interaction contrasts were evaluated for <u>happy valence</u> * identity:

3) $((happy_{OC} > neutral_{OC}) > (happy_{UC} > neutral_{UC}))$

4) $((happy_{OC} > sad_{OC}) > (happy_{UC} > sad_{UC}))$.

Given our *a priori* interest in dissociating and overlapping cortico-limbic regions, region-of-interest (ROI) analyses were conducted for the following regions: ventral striatum, anterior cingulate cortex, hippocampus, inferior frontal/orbito-frontal cortex, amygdala, and insula. Masks were obtained from the SPM AAL atlas (Automated Anatomical Labeling) provided by wfu pickatlas toolbox [18]. As the AAL atlas does not provide a mask for the ventral striatum, the central coordinates of the ventral striatum (x=±14, y=8, z=-8) were taken from an fMRI study targeting reward processing [19]. The ROI was created as an 8 mm sphere centered on this voxel. For all brain areas, we used a statistical threshold of $p<0.05$, corrected for multiple comparisons across the whole brain (family-wise error (FWE)). Coordinates are reported in MNI (Montreal Neurological Institute) space. Designations of anatomical regions

were based on the canonical T1-image provided by SPM and regions were identified using the WFU Pickatlas [18] and confirmed manually using a human brain atlas [20].

The ROI analyses were followed by exploratory whole-brain analyses (p<.001, uncorrected) to evaluate the context of the ROI findings. Finally, we conducted a conjunction analysis (conjunction null hypothesis method) based on the full-factorial analysis for the interaction contrasts ((sad$_{OC}$ > neutral$_{OC}$) > (sad$_{UC}$ > neutral$_{UC}$)) and ((happy$_{OC}$ > neutral$_{OC}$) > (happy$_{UC}$ > neutral$_{UC}$)) to determine common activation profiles of happy and sad faces of the own child across all subjects (p<0.05, FWE corrected).

Results

Behavioral Data

Response Times:

Mean response times and hit rates are shown in Table 1. We found a significant main effect for valence category ($F_{(2,50)}$=35.459, p≤.001; η^2=.59) with the lowest response times for happy faces (all p-values≤.001). The main effect for identity failed to reach significance ($F_{(1,25)}$=3.742, p=.130; η^2=.13), however, the valence by identity interaction was significant ($F_{(2,50)}$=6.919, p≤.01; η^2=.22) showing that mothers recognized happy faces of their own child faster than happy faces of the unfamiliar child ($t_{(25)}$=-6.928; p≤.001).

Hit Rates:

The main effect of valence category was significant ($F_{(2,50)}$=23.481, p≤.001; η^2=.48) with the highest accuracy for happy faces (all p-values≤.001). The main effect of identity ($F_{(1,25)}$=0.000, p=1.00; η^2=.00) and the valence by identity interaction ($F_{(2,50)}$=2.424, p=.09; η^2=.09) did not reach significance.

Valence ratings:

Mean valence and arousal ratings across the six picture conditions are shown in Table 1. We found a significant main effect of valence category ($F_{(2,52)}$=409.810, p≤.001; η^2=.94) with the highest valence ratings for happy and the lowest for sad faces (all p-values≤.001). The main effect of identity did not reach significance ($F_{(1,26)}$=2.797, p=.11; η^2=.10). However, the valence by identity interaction was significant ($F_{(2,52)}$=16.279, p≤.001; η^2=.39): Post-hoc tests revealed that maternal valence ratings were more negative for the own child compared to the unfamiliar child in the sad (mean difference=- .38; SD= .63; $t_{(26)}$=-3.168, p=.004) compared to neutral condition (mean difference= .00; SD= .71; $t_{(26)}$=-.027, p=.98). Similar results were found for happy faces: mothers rated faces of their own child more positive than of the unfamiliar child in the happy condition (mean difference= .70; SD= .62; $t_{(26)}$=5.786, p<.001) compared to the neutral condition (mean difference= .00; SD= .71; $t_{(26)}$=-.027, p=.98).

Arousal ratings:

There were significant main effects of valence category ($F_{(2,52)}$=37.722, p≤.001; η^2=.60) and identity ($F_{(1,26)}$=35.641, p≤.001; η^2=.58) with the lowest arousal ratings for neutral faces, highest arousal ratings for happy faces, and higher ratings for one's own child (all p-values≤.001). We found a significant valence by identity interaction ($F_{(2,52)}$=7.489, p≤.001; η^2=.22). Post-hoc tests revealed that maternal arousal ratings were higher for the own child compared to the unfamiliar child in the sad (mean difference= .85; SD= .96; $t_{(26)}$=4.582, p<.001) compared to neutral condition (mean difference= .41; SD= .60; $t_{(26)}$=3.645, p=.001). Similar results were found for happy faces: maternal arousal ratings were higher for the own child compared to the unfamiliar child in the happy (mean difference= 1.0; SD= .77; $t_{(26)}$=6.552, p<.001) compared to neutral condition (mean difference= .41; SD= .60; $t_{(26)}$=3.645, p=.001).

Neuroimaging Data

*sad valence * identity interaction*

In a first step, we studied the effect of sad facial expressions (of the own child) by contrasting the effect of sad versus neutral valence in pictures of the own (versus unfamiliar) child (i.e., valence (sad vs. neutral) * identity (own vs. unfamiliar) interaction). The ROI analyses (p<.05, FWE corrected) indicated significant activations in the amygdala, the insula, the hippocampus, and the anterior cingulate cortex (Table 2; Figure 1). In addition to these regions, the exploratory whole-brain analysis (p<.001, uncorrected) revealed clusters in the frontal gyrus, superior temporal gyrus, putamen, (pre)cuneus, and parahippocampal regions (Table 2). Maternal valence ratings for their own sad child and peak voxel BOLD responses in the anterior cingulate cortex were negatively correlated (r=-.413, p=.032), indicating that more negative ratings of the own sad child were associated with greater activation in the anterior cingulate cortex.

In a second step, we examined dissociable effects of sad versus happy facial expressions (of the own child). For this purpose, we contrasted the effect of sad versus happy valence in pictures of the own (versus unfamiliar) child (i.e., valence (sad vs. happy) * identity (own vs. unfamiliar) interaction). The ROI analyses (p<.05, FWE corrected) indicated almost identical results as in the first interaction term involving neutral faces, i.e., effects in the amygdala, insula, hippocampus, and the anterior cingulate cortex (Supplementary Table 1). The exploratory whole-brain analysis (p<.001, uncorrected) revealed additional activations in the inferior orbito-frontal gyrus, superior temporal gyrus, precuneus, and parahippocampal regions.

*happy valence * identity interaction*

In a first step, we studied the effect of happy facial expressions (of the own child) by contrasting the effect of sad versus neutral valence in pictures of the own (versus unfamiliar) child (i.e., valence (happy vs. neutral) * identity (own vs. unfamiliar) interaction). The ROI analyses indicated significant activations in the left hippocampus ($p<.05$, FWE corrected) (Table 3; Figure 2). The exploratory whole-brain analysis ($p<.001$, uncorrected) for the happy valence * identity effect revealed additional bilateral activation in the insula, superior temporal gyrus, inferior frontal gyrus, inferior parietal gyrus, the right parahippocampal region, and the right precuneus.

In a second step, we examined dissociable effects of happy versus sad facial expressions (of the own child). For this purpose, we contrasted the effect of happy versus sad valence in pictures of the own (versus unfamiliar) child (i.e., a valence (happy vs. sad) * identity (own vs. unfamiliar) interaction). The ROI analysis ($p<.05$, FWE corrected) did not indicate significant results. However, our exploratory whole-brain analysis ($p<.001$, uncorrected) indicated similar activation as in the first happy valence * identity interaction, i.e., effects in the inferior frontal gyrus, the inferior parietal gyrus, and the right parahippocampus (Supplementary Table 2).

Conjunction analysis

A conjunction analysis was carried out based on the interaction contrasts $((happy_{OC} > neutral_{OC}) > (happy_{UC} > neutral_{UC}))$ and $(sad_{OC} > neutral_{OC}) > (sad_{UC} > neutral_{UC})$ to examine common neural responses to sad and happy facial expressions. The ROI analysis ($p<.05$, FWE corrected) yielded significant activation in the insular region. The exploratory whole brain analysis ($p<.001$, uncorrected) showed additional overlapping effects in the superior and middle frontal gyrus, middle cingulate gyrus, superior temporal gyrus, cuneus, and (para-) hippocampal regions (Table 4; Figure 3).

Discussion

The aim of the present study was to examine dissociable and overlapping activations for sad and happy faces of the own (compared to an unfamiliar) child. Our paradigm is one of the first that allows one to directly compare sad and happy faces of the own child. We found that viewing one's own sad child activated the amygdala, anterior cingulate cortex, insula, and hippocampus, which may be considered areas of a threat detection network. In contrast, viewing one's own happy child did not activate the amygdala and anterior cingulate cortex, but the (para)hippocampus, insula, precuneus, and inferior frontal gyrus, i.e., areas which may be considered part of a reward network. Overlapping activations for sad and happy faces of the own child included the insula and superior temporal gyrus, which may relate to

an empathy network. Our findings suggest that affect recognition of sad and happy facial expressions of the own child activates overlapping and dissociable networks, which might lay the foundations for sensitive maternal behavior with differential maternal responses to distinct child emotions.

Most previous studies on maternal perception of the own child's face have relied on neutral and happy facial expressions [6-8] and found activation in the orbitofrontal cortex, striatum, thalamus, and hypothalamus. Going one step further, in the present study, we also studied maternal responses to sad child faces and found activation in the amygdala, anterior cingulate cortex, insula, and hippocampus which have been associated with a variety of processes, including fear processing [21], salience detection [22], and empathizing with the pain of a loved one [23]. One may tentatively suggest that recognizing the own child's sad face activates a threat detection network in the mother [4, 24, 25].

Only few previous studies have presented sad child expressions to mothers [9, 10] relying on infant faces. One of these studies [9] found that sad faces of the own child elicit a stronger amygdala response compared to an unknown child. Another line of research has studied maternal responses to sad auditory infant stimuli, i.e., baby cry. Also these studies found maternal activation in the amygdala, anterior cingulate cortex, and insula [26-29]. Our present study differs from these previous visual and auditory studies in that we used pictures of school-aged children as opposed to infants. Thus our children were presumably less dependent of and attached to their mothers. Nonetheless, we again found strong activation in the amygdala, anterior cingulate cortex, and insula indicating the high salience of the own child's sad face for a mother, which may exist independent of the child's age. The question arises whether maternal responses to their own child's sad affective states alter when they grow up further. To address this issue, it would be desirable to study mothers' neural responses to children above 12 years.

One of the challenges in studying maternal neural responses to their child's affective states is to combine both happy and sad states in one paradigm. For reasons of feasibility, visual studies may primarily have focused on happy facial expressions and auditory studies on infant cry. Sad facial expressions in children and happy auditory stimuli in infants may be more difficult to establish. Relying on school children, the present study was in the position to develop a paradigm that included both happy and sad facial expressions of children. The present paradigm therefore adds to the literature in that it allows studying the direct comparison of neural response to sad and happy child faces.

While sad faces produced activations in the amygdala and ACC, happy faces (own versus unfamiliar child) produced activation in the inferior frontal gyrus, precuneus, and

(para)hippocampus. These latter regions have been associated with reward processing [5, 30] as well as the retrieval of person knowledge and episodic memories [31-33].

Our behavioral data showed that mothers recognized pictures of happy faces of their own child faster and rated them as more arousing compared to the unfamiliar child. The question arises whether happy child faces were easier to recognize and therefore induced stronger BOLD signals than sad child faces. This would not affect our results for sad faces nor the conjunction analysis. However, for the contrast of happy faces of the own child compared to sad faces (compared to the unfamiliar child) this could potentially confound the findings. To address this issue, we performed an additional second-level full-factorial analysis including response times and arousal ratings as covariates. This analysis, again showed significant activations in the inferior frontal gyrus, inferior parietal gyrus, and the right parahippocampus ($p<.001$, uncorrected) in response to happy faces, suggesting that findings in the happy condition are not confounded by better perceptibility of happy faces.

From an evolutionary perspective, it is likely that specific brain mechanisms in mothers have developed to secure the survival of their offspring. Different stages of processing may be distinguished in maternal responses to their child's affective states, starting from early (subcortical) visual information processing through more complex (cortical/prefrontal) perceptive processes to motor actions. At the same time, it is obvious that adequate maternal responses to sad and happy affective states will differ. Our data from the affect recognition task (requiring perception but not motor action) indicate that this difference is already present during perceptive stages of the maternal responses, even during early subcortical visual information processing. It may be speculated that these early differential responses to sad and happy faces may facilitate fast and adequate reactions of the mothers, e.g., vigilant protective behavior in response to sad child faces and sensitive parenting behavior in response to happy, rewarding child faces.

In addition to dissociable networks, our paradigm also allowed us to identify brain areas showing overlapping activations to both happy and sad facial expressions of the own child. We found activation in areas associated with cognitive and affective aspects of empathy, such as the superior temporal gyrus and the insular regions [34-37]; for a meta-analysis, see [38]. The common network possibly reflects healthy mothers' ability to understand their child's intentions and wishes, and to react sensitively to them.

In conclusion, mothers showed dissociable and overlapping activations in response to sad and happy facial expressions of the own child. Sad facial expressions activated a threat detection network (including the amygdala and anterior cingulate cortex). Happy facial expressions of the own child activated a reward network (including inferior frontal gyrus, precuneus, and (para)hippocampus). Common activation of sad and happy facial expressions activated an empathy network (including the insula and superior temporal

gyrus). Our data indicate that mothers activate these networks not only in response to infants', but also to school children's affective states. Our data also suggest that dissociable responses to sad and happy facial expressions can already be observed during perceptive stages of the maternal responses, even during early subcortical visual information processing. Altered activation of these neural networks might negatively impact parenting behavior. This has to be shown in future studies including mothers-child dyads showing dysfunctional interaction.

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All authors declare that they have no conflicts of interest related to this work and that they approve the final manuscript.

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Table 1: Behavioral data across picture conditions

	Response times[a]		Hit rates[b]		Valence ratings[c]		Arousal ratings[d]	
Picture condition	Mean	SD	Mean	SD	Mean	SD	Mean	SD
OC neutral	1118.3	162.2	78.8	15.8	4.1	0.6	4.1	0.7
OC happy	808.0	102.8	99.9	0.7	6.6	0.4	5.8	1.1
OC sad	1008.2	191.8	90.6	12.3	2.5	0.6	5.1	1.0
UC neutral	1057.8	156.6	84.1	15.5	4.0	0.4	3.7	0.8
UC happy	877.0	82.4	91.0	12.3	5.9	0.6	4.8	1.1
UC sad	1081.7	243.0	87.3	13.1	2.9	0.6	4.2	1.1

OC: own child; UC: unfamiliar child; SD: standard deviation

a in ms

b percentage of correct answers

c rated 1-7, with 1 being most negative and 7 being most positive

d rated 1-7, with 1 being least arousing and 7 being most arousing

Table 2: Results for the contrast: (sad_oc > neutral_oc) > (sad_uc > neutral_uc)

			MNI coordinates			
Region	BA	R/L	x	y	z	T value
Frontal						
Superior frontal gyrus[b]	9	L	-20	24	42	5.87
Middle orbitofrontal gyrus[b]	10	R	2	46	-8	6.98
Anterior cingulate gyrus[a]	32	L	-8	30	-8	5.69
	32	R	0	52	-2	6.48
Precentral gyrus[b]	44	R	50	0	6	5.66
Temporal						
Posterior superior temporal gyrus[b]	39	L	-54	-56	8	5.07
Middle temporal gyrus[b]	21	L	-58	-10	-22	8.22
Putamen[b]	21	R	58	-10	-22	6.50
Parietal						
Posterior cingulate/Precuneus[b]	31	L	-2	-54	28	6.64
Inferior parietal gyrus[b]	40	L	-62	-30	26	5.74
	40	R	52	-30	26	5.74
Postcentral gyrus	3	R	38	-34	68	6.10
Occipital						
Cuneus[b]	19	L	-12	-90	24	5.04
	18	R	6	-84	22	5.19
Middle occipital gyrus[b]	39	R	48	-66	24	5.07
Subcortical						
Amygdala[a]		L	-28	-4	-24	4.03
		R	26	-2	-28	4.56
Hippocampus[a]		L	-26	-10	-24	5.80
		R	28	-14	-22	5.52
Parahippocampal gyrus[b]	36	L	-24	-30	-18	4.78
	35	R	22	-4	-28	5.72
Insula[a]	13	L	-38	-6	-8	5.42
	13	R	36	4	8	5.13

p<.001 uncorrected; BA: Brodman's area; R: right, L: left; MNI: Montreal Neurological Institute; [a]p<.05 (FWE), corrected for small volume (SVC); [b]p<.05 (FWE), corrected for whole-brain volume

Table 3: Results for the contrast: (happy_oc > neutral_oc) > (happy_uc > neutral_uc)

			MNI coordinates			
Region	BA	R/L	x	y	z	T value
Frontal						
Superior frontal gyrus	32	L	-18	8	46	4.05
Middle frontal gyrus	8	R	28	26	48	3.66
Inferior frontal gyrus	13	R	38	12	12	3.92
Middle cingulate gyrus	31	L	-12	-30	38	3.45
	31	R	14	-34	38	3.25
Temporal						
Superior temporal gyrus[b]	22	L	-50	-4	4	4.87
	41	R	50	-30	15	5.57
Inferior temporal gyrus	20	R	58	-4	-30	3.56
Parietal						
Inferior parietal gyrus[b]	41	L	-50	-34	22	6.43
Precuneus		R	10	-50	5	3.14
Occipital						
Middle occipito-temporal gyrus[b]	19	L	-16	-52	-8	5.31
Cuneus[b]	19	R	6	-84	26	7.07
Subcortical						
Insula[a]	13	L	-44	-2	-6	4.16
	13	R	38	-14	14	4.38
Hippocampus[a]		L	-30	-30	-12	3.37
Parahippocampal gyrus[b]	36	R	20	-44	-4	4.33

p<.001 uncorrected; BA: Brodman's area; R: right, L: left; MNI: Montreal Neurological Institute; [a]p<.05 (FWE), corrected for small volume (SVC); [b]p<.05 (FWE), corrected for whole-brain volume

Table 4: Results for the conjunction analysis

Region	BA	R/L	MNI coordinates x	y	z	T value
Frontal						
Superior frontal gyrus	6	L	-18	8	46	4.05
Middle frontal gyrus	8	R	28	26	48	3.66
Middle cingulate gyrus	31	R	14	-34	38	3.25
Temporal						
Superior temporal gyrus[b]	40	L	-52	-34	20	5.73
	22	R	54	-2	-2	4.97
Inferior temporal gyrus	20	R	58	-4	30	3.56
Parietal						
Inferior parietal gyrus	40	L	-56	-48	46	3.19
Occipital						
Cuneus[b]	18	R	6	-84	22	5.19
Subcortical						
Insula[a]	22	L	-50	-4	4	4.87
	13	R	46	-32	20	5.54
Hippocampus		R	-30	-30	-12	3.37
Parahippocampus	35	L	-30	-32	-14	3.29

p<.001, uncorrected; BA: Brodman's area; R: right, L: left; MNI: Montreal Neurological Institute; [a]p<.05 (FWE), corrected for small volume (SVC); [b]p<.05 (FWE), corrected for whole-brain volume

Caption of figure 1

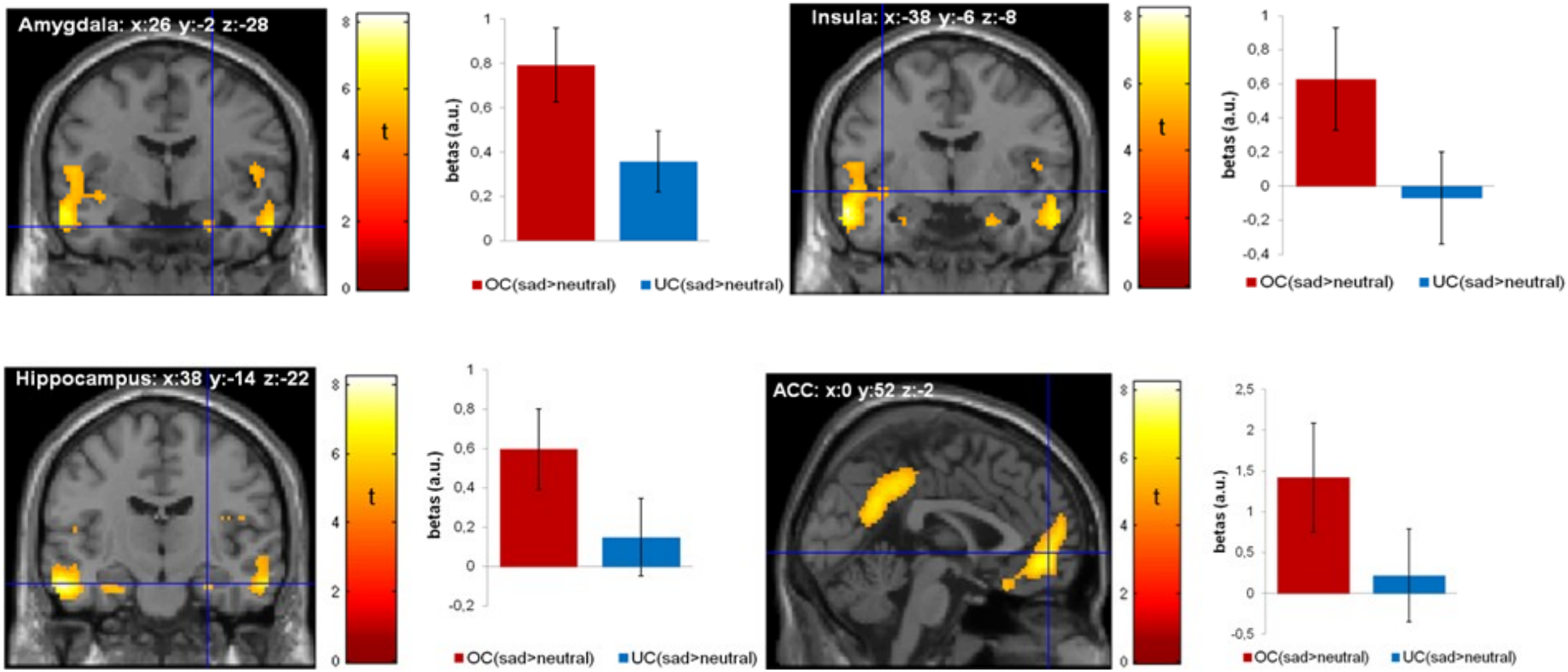

Figure 1: activation maps for the contrast ((sad_OC > neutral_OC) > (sad_UC > neutral_UC)) are thresholded at p<0.05 (FWE corrected) and overlayed on a standard MRI template; bar plots represent the peak voxel parameter estimates, error bars represent one standard error of the mean; a.u.: arbitrary units; OC: own child; UC: unfamiliar child; ACC: anterior cingulate cortex;

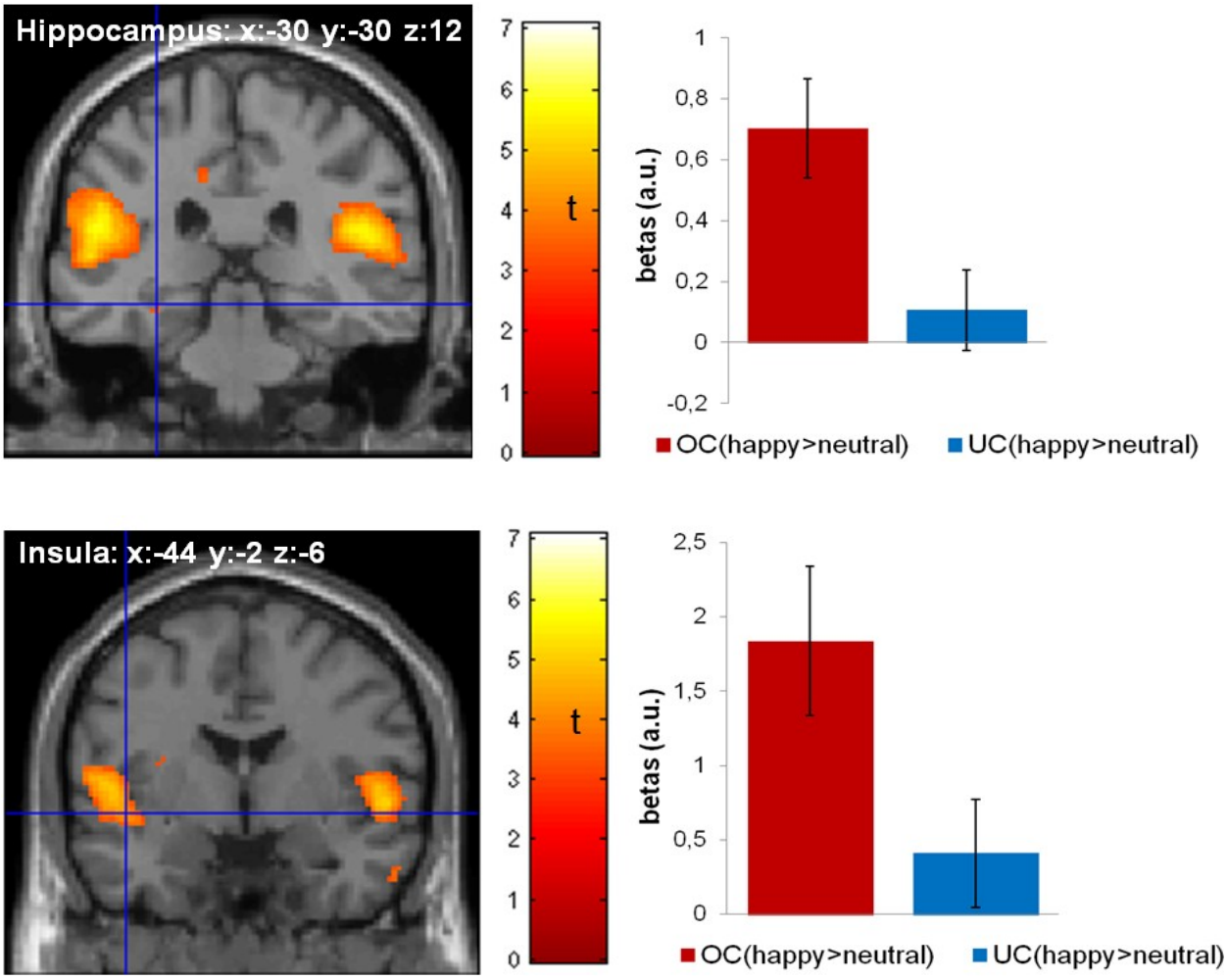

Figure 2: activation map for the contrast ((happy_OC > neutral_OC) > (happy_UC > neutral_UC)) is thresholded at p<0.05 (FWE corrected) and overlayed on a standard MRI template; bar plots represent the peak voxel parameter estimates, error bars represent one standard error of the mean; a.u.: arbitrary units; OC: own child; UC: unfamiliar child;

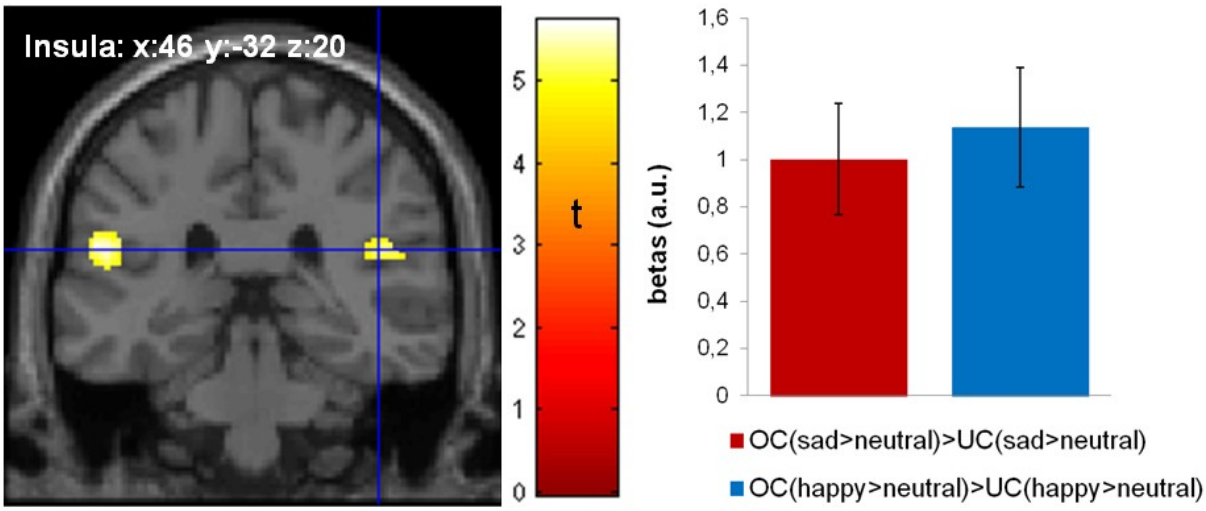

Figure 3: activation map for the conjunction analysis is thresholded at p<0.05 (FWE corrected) and overlayed on a standard MRI template; bar plots represent the peak voxel parameter estimates, error bars represent one standard error of the mean; a.u.: arbitrary units; OC: own child; UC: unfamiliar child;

Supplemantary Table 1: Results for the contrast: (sad_oc > happy_oc) > (sad_uc > happy_uc)

Region	BA	R/L	MNI coordinates x	y	z	T value
Frontal						
Middle orbitofrontal gyrus[b]	10	L	-2	46	-10	9.33
Inferior orbitofrontal gyrus[a]	10	L	-30	30	-18	5.22
	47	R	24	16	-22	5.78
Anterior cingulate gyrus[a]	32	L	-2	42	-6	8.68
	32	R	4	16	22	4.95
Temporal						
Middle temporal gyrus[b]	21	L	-58	-10	-20	8.36
	21	R	40	20	-36	5.17
Parietal						
Posterior cingulate gyrus[b]	31	L	-4	-54	28	9.22
Precuneus[b]	31	L	-6	-54	26	9.02
Postcentral gyrus	3	R	40	-36	68	5.60
Occipital						
Fusiform gyrus	37	L	-32	-36	-18	5.51
Subcortical						
Amygdala[a]		L	-28	-4	-22	4.94
		R	26	-2	-28	4.94
Hippocampus[a]		L	-26	-6	-24	4.75
		R	26	-4	-24	4.83
Parahippocampal gyrus[b]	35	R	24	-2	-28	4.99
Insula[a]	47	L	-28	10	-20	3.96
	47	R	26	14	-20	5.15

p<.001 uncorrected; BA: Brodman's area; R: right, L: left; MNI: Montreal Neurological Institute; [a]p<.05 (FWE), corrected for small volume (SVC); [b]p<.05 (FWE), corrected for whole-brain volume

Supplementary Table 2: Results for the contrast: (happy_oc > sad_oc) > (happy_uc > sad_uc)

			MNI coordinates			
Region	BA	R/L	x	y	z	T value
Frontal						
Superior frontal gyrus	6	R	8	28	40	4.68
Middle frontal gyrus	8	R	44	16	48	3.83
	8	L	-38	50	0	3.56
Inferior frontal gyrus[b]	13	R	40	32	28	3.91
Supplemental motor area	32	L	2	22	46	4.36
Parietal						
Inferior parietal gyrus	41	L	-42	-40	42	3.51
Angular gyrus	40	R	38	-54	38	3.15
Occipital						
Lingual gyrus	19	R	20	-60	2	4.33
Subcortical						
Parahippocampal gyrus	36	R	20	-44	-4	3.30

p<.001 uncorrected; BA: Brodman's area; R: right, L: left; MNI: Montreal Neurological Institute; [a]p<.05 (FWE), corrected for small volume (SVC); [b]p<.05 (FWE), corrected for whole-brain volume

7.1.2 Study II

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Title: Transgenerational effects of maternal depression on affect recognition in children

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Abstract

Background

The association between maternal depression and adverse emotional and behavioral outcomes in children is well established. One associated factor might be altered affect recognition which may be transmitted transgenerationally. Individuals with history of depression show biased recognition of sadness. Our aim was to investigate parallels in maternal and children's affect recognition with remitted depressed mothers.

Methods

60 mother-child dyads completed an affect recognition morphing task. We examined two groups of remitted depressed mothers, with and without history of physical or sexual abuse, and a group of healthy mothers without history of physical or sexual abuse. Children were between 5 and 12 years old.

Results

Across groups, mothers identified happy faces fastest. Mothers with remitted depression showed a higher accuracy and response bias for sadness. We found corresponding results in their children. Maternal and children's bias and accuracy for sadness were positively correlated. Effects of remitted depression were found independent of maternal history of physical or sexual abuse.

Limitations

Our sample size was relatively small and further longitudinal research is needed to investigate how maternal and children's affect recognition are associated with behavioral and emotional outcomes in the long term.

Conclusions

Our data suggest a negative processing bias in mothers with remitted depression which might represent both the perpetuation of and vulnerability to depression. Children of remitted depressed mothers appear to be exposed to this processing bias outside acute depressive episodes. This may promote the development of a corresponding processing bias in the children and could make children of depressed mothers more vulnerable to depressive disorders themselves.

Keywords: maternal depression, transgenerational transmission, morphing task, affect recognition

1) Introduction

There is ample empirical evidence for an association between maternal depression and a range of adverse child behavioral (Lee & Gotlib, 1991) and emotional outcomes (for review, see: (Beardslee, Gladstone, & O'Connor, 2011; Goodman et al., 2011). Children of depressed parents often show diminished affect regulation and cognitive and language functioning when their mothers are depressed (e.g., Carter et al., 2001; Cicchett et al., 1998; Rohde et al., 2005). They are at risk for developing depressive disorders themselves (Sim & England, 2009) and other internalizing and externalizing disorders (Lyons-Ruth et al., 1997). However, the factors contributing to the transgenerational transmission of depression have not been fully elucidated. One psychological factor contributing to the risk of transmission might be altered affect recognition in mothers, such as difficulties in correctly interpreting and responding to facial expressions.

In adults, a number of studies have investigated alterations in facial affect recognition in depression. These studies consistently showed an increased accuracy of, and increased response bias for sad faces (Arteche et al., 2011; Gollan et al., 2010; Gollan et al., 2008; Gur et al., 1992; Hale, 1998; Lee et al., 2008; Mandal & Bhattacharya, 1985; Sterzer et al., 2011; Surguladze et al., 2004). These emotional-cognitive deficits seem to persist during remission (Bhagwagar & Cowen, 2008; Bouhuys et al., 1999; Fuhr et al., 2014; Joormann & Gotlib, 2007; Lange et al., 2012). The question arises whether biased affect recognition might be transmitted from affected mothers to their children. Investigations addressing this question have only recently begun and suggest that alterations in affect recognition may also exist in children of depressed mothers. The alterations seem mainly to concern sad affects (Joormann et al., 2010; Lopez-Duran et al., 2013). To the best of our knowledge, to date no studies exist that have directly investigated parallels in affect recognition in mother-child dyads.

We here studied affect recognition in both mothers with remitted depression and their children to address the question of whether biased affect recognition in remitted depressed mothers corresponds with respective alterations in their children.

Patients with depression often report a history of traumatization, such as physical or sexual abuse (Heim et al., 2008; Lizardi et al., 1995; McCabe et al., 2009). Based on neurobiological (Heim et al., 2008; Vythilingam et al., 2002) and treatment studies (Nemeroff et al., 2003), it has been suggested that depressed patients with and without trauma represent two distinct subgroups of depression. This distinction may be critical for the investigation of affect recognition, as history of trauma has – independently of depression - been associated with altered affect recognition. However, these alterations seem to concern biased anger and fear processing mainly (Dannlowski et al., 2012; Poljac et al., 2011; Rauch et al., 2000; Shin et al., 2005; van Harmelen et al., 2010). To account for effects of

trauma, we here distinguished between remitted depressed mothers with and without history of trauma (i.e., physical or sexual abuse).

We tested two hypotheses in the present study. First, we predicted that mothers with remitted depression would exhibit higher accuracy and a response bias for sad faces. Second, we hypothesized that children of remitted depressed mothers would show corresponding alterations.

To study these hypotheses we performed an affect recognition task in mothers with remitted depression and their children. We tested for parallels between mothers and children both at group and at dyadic level. At group level, we investigated whether group differences observed between depression and control mothers were analogously found in children. At dyadic level, we examined whether maternal and children's abilities in affect recognition for sad facial expressions were correlated.

2) Methods

2.1. Participants

The current study involved 81 mothers (N=23 healthy controls, N=20 remitted depression only, N=38 remitted depression with trauma) and their children (n=16 of healthy control mothers, n=15 of remitted depressed mothers, n=29 of remitted depressed mothers with history of trauma). Mean time elapsed since last depressive episode was 54.7 months (range: four to 318 months). Mean number of depressive episodes was 2.2 (range: one to six). The majority (84.0%) of remitted depressed mothers had received psychotherapeutic treatment and half of them (48.0%) had received psychiatric treatment. Approximately, one third of them (32.0%) had been hospitalized at least once for their depression. Unequal sample sizes between maternal and child groups are due to a later implementation of the child morphing task in our study. Groups did not differ with respect to demographic variables, IQ, and maternal HAMD (Hamilton, 1960; 1976) scores (see also Table 1 for sample demographic characteristics).

Mothers were recruited by advertisement (e.g., psychiatric and gynecological outpatient clinics). Mother and child had to live together, also in the case of shared custody of the child. Children were between 5 and 12 years old and attended primary school. Mothers' HAMD scores had to be below seven to ensure full remission of depression (Rush et al., 2006). In mothers, exclusion criteria were neurological diseases, consumption of benzodiazepines within the last 6 months, acute axis I disorders, history of schizophrenia or manic episodes, and the following three personality disorders: emotional-unstable, anxious-avoidant, and antisocial personality disorder. Children were required to have an IQ score above 70.

We recruited three study groups: 1) Healthy control mothers without history of psychiatric disorders and without history of physical or sexual abuse, 2) remitted depressed mothers without history of physical or sexual abuse, and 3) remitted depressed mothers with additional history of physical or sexual abuse. The present study was performed within the framework of the UBICA ("Understanding and Breaking the Intergenerational Cycle of Abuse") multicenter project which investigates the effects of maternal trauma on mother-child interaction and child wellbeing. The study reported here was an add-on to this UBICA project, i.e. it was carried out in a subgroup of mother-child dyads that did also participate in the UBICA study. Findings of the UBICA study will be reported elsewhere..

Nine mothers were excluded as their response times and hit rates fell outside two standard deviations of the sample mean (n=2 healthy controls, n=2 remitted depressed without trauma, n=5 remitted depressed with trauma). Datasets of five children were excluded from analyses for the same reason (n=2 children of healthy controls, n=1 child of a remitted depressed mother without trauma, n=2 children of remitted depressed mothers with trauma). At group level, we included data of 72 mothers and 55 children for analysis. At dyadic level, a total of 55 mother-child dyads were included for analysis.

2.2. Procedure

During the first study session, mothers performed the affect recognition task. In addition, the M.I.N.I. (Mini International Neuropsychiatric Interview; Lecrubier et al., 1997) and the IPDE (International Personality Disorder Examination; Loranger, 1999) were conducted to establish mothers' diagnoses of acute and lifetime DSM-IV axis I and II disorders. To rule out residual depressive symptomatology, we applied the HAMD interview (Hamilton, 1960). To rule out differences in maternal intellectual abilities, we used a German vocabulary test (Wortschatztest, WST; Schmidt & Metzler, 1992).

During the second study session, history of maternal childhood trauma was assessed using the CECA interview (Childhood Experience of Care and Abuse; Bifulco et al., 1994) which is regarded as the golden standard in retrospective assessment of childhood maltreatment (Thabrew et al., 2012). A score of "moderate" to "severe" on either the "physical abuse" or the "sexual abuse" subscale was considered as an indicator for childhood trauma. Additional information was obtained on the occurrence and severity of further sexual and physical abuse during adulthood, applying adapted questions and coding rules of the CECA.

Children performed the affect recognition task during the second study session. Children's intellectual abilities were assessed using either the Culture Fair Intelligence Test I revised for children (CFT 1-R; age 5-8; Weiss & Osterland, 1997), or the CFT 20-R (age 9-12; Weiss et al., 2006).

The study was approved by the ethics committee of the Charité – Universitätsmedizin Berlin. Written informed consent was obtained from all participants.

2.3. Affect recognition task

The affect recognition task used computer-manipulated images of adult faces, whose expression (0%) gradually (increments of 1%) and continuously (10 increments per sec) morphed from neutral to happy, sad, angry, or fearful (100%). Modifications of this task have previously been studied by Domes and colleagues (Domes et al., 2008; Lischke et al., 2012; Matzke et al., 2014). For the current version of the task, photos from four female and four male adults were taken from the Karolinska Database of Emotional Faces (Lundqvist et al., 1998). For the adult version of the task, a total of 64 trials (16 for each affect, i.e., happy, sad, angry, fearful) were presented in a random order on a 15.6 inch laptop monitor placed at approximately 55 cm distance from participants' eyes. Participants were asked to press a stop button as soon as they recognized the emerging affect. They then selected one of the four affects by button press (forced choice). A time-limit of two seconds was set for the selection of the affect category. The task was programmed using the MATLAB toolbox Cogent 2000 (developed by the Cogent 2000 team) running on MATLAB 7.1 (The MathWorks Inc., Natick, MA, 2000).

Children performed the same task as their mothers, with two modifications: to shorten the task duration, the child version of the task did not include the affect category of fear and only comprised a total of 36 trials (12 for each affect, i.e., happy, sad, and angry). The children were also required to press a stop button as soon as they recognized the emerging affect, but depending on their age, they could select the affect category either by button press or verbally. For the child task, no time limit was set for the selection of the affect category.

All participants performed four practice trials to familiarize themselves with the task.

The following outcome variables were analyzed:

1) Response times for presses of the stop button in correct trials.

2) An accuracy score. This was preferred to hit rates, because hit rates can be affected by response tendencies to one affect: for instance, a subject would achieve a high hit rate for sad facial expressions when always selecting "sad". The accuracy score was calculated for each affect category separately. Specifically, the number of correct answers for a given affect category was divided by the number of all correct answers (e.g., accuracy for sadness in percent = [(number of correct answers for sadness/number of correct answers for all affects)*100]).

3) A response bias, which reflects the systematic tendency to misinterpret facial expressions in favor of a certain affect category. For instance, the response bias for sadness concerns the tendency to (incorrectly) categorize happy, angry, and fearful faces as sad (bias for sadness in percent = [Σ(number of happy faces misinterpreted as sad + number of angry faces misinterpreted as sad + number of fearful faces misinterpreted as sad) / (number of all incorrect answers)*100]).

2.4. Statistical Analysis

For all analyses, the statistical significance threshold was set at $p<.05$. At group level, we used repeated-measures analyses of variance (ANOVA) to test our hypotheses regarding group differences with affect category as within-subject factor and group as between-subject factor. Degrees of freedom were Greenhouse-Geisser corrected whenever necessary (Abdi, 2010; Geisser & Greenhouse, 1958) (for clarity, the uncorrected degrees of freedom are reported). Post-hoc single comparisons were carried out using separate t-tests. At dyadic level, we also correlated maternal and children's affect recognition abilities using two-tailed Pearson's correlations. All calculations were conducted using SPSS for Windows (Version 18).

3) Results

3.1. Response Times

Mothers: In mothers, we did not find a main effect of group ($F_{(2,69)}=2.619$, $p>.05$; $\eta^2=.07$), but the main effect of affect was significant ($F_{(3,207)} = 446.002$, $p\leq.001$; $\eta^2=.87$): participants identified happy faces earlier compared to the other affects. This was consistent across groups indicated by a non-significant group by affect interaction ($F_{(6,207)}=1.201$, $p>.05$; $\eta^2=.034$).

Children: In children, we did not find a main effect of group ($F_{(2,52)}=0.007$, $p>.05$; $\eta^2=.00$), but the main effect of affect was significant ($F_{(2,104)}=86.525$, $p\leq.001$; $\eta^2=.625$), with children identifying happy faces earlier than sad and angry faces. The group by affect interaction did not yield significance ($F_{(4,104)}=1.541$, $p>.05$; $\eta^2=.056$).

3.2. Accuracy

Mothers: With regard to accuracy, we did not find a significant main effect of group ($F_{(2,69)}=2.135$, $p>.05$; $\eta^2=.09$). Across groups, there was a significant main effect of affect category ($F_{(3,207)}=50.173$, $p\leq.001$; $\eta^2=.421$) with the highest accuracy for happy faces. We found a significant interaction term

($F_{(6,207)}$=2.442, p<.027; η^2=.066): post-hoc analyses revealed that remitted depressed mothers, either with ($t_{(52)}$=-2.715, p=.009) or without trauma ($t_{(37)}$=-2.087, p=.044), showed a greater sadness accuracy (Figure 1a). In addition, mothers with both, remitted depression and history of trauma, had lower accuracy scores for fearful expressions compared to healthy controls ($t_{(52)}$=2.549, p=.014) which might reflect attentional avoidance of fear (Poljac et al., 2011).

Children: We did not find a significant main effect of group ($F_{(2,52)}$=1.630, p>.05; η^2=.06). Across groups there was a significant main effect of affect category ($F_{(2,104)}$=44.956, p≤.001; η^2=.465) with the highest accuracy for happy faces. The group by affect interaction failed to reach significance ($F_{(4,104)}$=1.868, p=.122; η^2=.067) (Figure 1b).

Mother-child dyad: However, there was a significant positive correlation across groups between maternal and children's sadness accuracy (r=.26, p=.045) (Figure 1c). After controlling for history of trauma, the correlation remained significant (r=.27, p=.048). Within groups, the correlations were not significant (control: r=.23, p>.05; depression only: r=.14, p>.05; depression and trauma: r=.28, p>.05).

3.3. Response bias

Mothers: For the maternal response bias in incorrect trials there was no significant main effect of group ($F_{(2,69)}$=1.594, p>.05; η^2=.04). The main effect of affect was significant ($F_{(3,207)}$=34.390, p<.001; η^2=.333) with the highest bias for anger and the lowest bias for happiness. We found a significant group by affect interaction ($F_{(6,207)}$=2.389, p=.046; η^2=.065): remitted depressed mothers with history of trauma showed a greater response bias for sad faces relative to the control mothers ($t_{(52)}$=-2.594, p=.012). Mothers with depression only showed a trend for the same effect ($t_{(37)}$=-1.797, p=.081) (Figure 2a). Compared to healthy controls, both depression groups also showed a reduced response bias for fearful faces (depression only: $t_{(37)}$=2.416, p=.021; depression and trauma: $t_{(52)}$=2.479, p=.016).

Children: For children, we found corresponding results (Figure 2b): the main effect of group did not yield significance ($F_{(2,52)}$=2.441, p>.05; η^2=.09), but we found a main effect of affect ($F_{(2,104)}$=14.232, p≤.001; η^2=.215): children showed the lowest response bias for happy faces. In addition, we found a significant group by affect interaction: $F_{(4,\ 104)}$=2.875, p=.026; η^2=.100. Similar to their mothers, children of mothers with remitted depression, either with ($t_{(39)}$=-2.580, p=.014) or without trauma ($t_{(26)}$=-2.713, p=.012), showed a greater sadness bias compared to children of healthy controls.

Mother-child dyad: There was also a trend-level significant positive correlation across groups between maternal and children's sadness bias (r=.24, p=.066) (Figure 2c). After controlling for history of trauma, the correlation reached significance (r=.30, p=.042). Within groups, the correlations were not significant (control: r=.24, p>.05; depression only: r=.43, p>.05; depression and trauma: r=.17, p>.05).

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4) Discussion

This present study used a morphing task to investigate facial affect recognition in remitted depressed mothers and their children. We found striking parallels between mothers and children both at group and at dyadic level. At group level, mothers with depression in remission showed a negative processing bias during affect recognition, which was paralleled in their children who showed a similar sadness bias. At dyadic level, we found a positive correlation between maternal and child sadness accuracy and – at trend level – sadness bias. Findings did not differ between depression groups with and without trauma. Our findings could possibly point to a transgenerational transmission process.

4.1. Affect recognition in mothers with a history of depression

Previous studies on affect recognition in acutely depressed patients have reported a negative processing bias in affect recognition, with increased accuracy and response bias for negative affects (Gollan et al., 2008; Gur et al., 1992; Hale, 1998; Lee et al., 2008; Mandal & Bhattacharya, 1985; Surguladze et al., 2004). Adding to this literature, we here found similar alterations of sad affect recognition in patients remitted from depression. While response times did not show group differences for trials of sad facial expressions in our study, we found greater accuracy scores in remitted depressed mothers during sad trials, as well as a greater response bias during trials where other affects are misinterpreted as sad. One may thus conclude that altered affect recognition in remitted depression can be detected both in presence (greater accuracy) and absence (misinterpretation of other affects) of sad faces.

Our findings in remission are in line with earlier studies showing altered affect recognition during remission (Lange et al., 2012) as well as with cognitive theories of depression (Beck, 1964, 2002; Teasdale, 1988) postulating that the onset, maintenance, and recurrence of depressive episodes are strongly related to biases in negative information processing. In accordance with these theories, our findings suggest that this bias represents a trait rather than a state marker of depression, which may increase the vulnerability for the development and recurrence of depression (Mathews & MacLeod, 2005) and impact on the offspring.

4.2. Affect recognition in children of remitted mothers

Children of both depression groups (i.e., with and without trauma) showed a response bias for sadness, similar to their mothers. In addition, we found a correlation between maternal and child sadness accuracy as well as (trendwise) between maternal and child sadness bias. This correlation was observed in across-groups analyses, but not in within-group analyses. The question arises whether the observed correlation may be related to a true dyadic linear relationship (independent of group assignment) or rather to a primary group effect. In the latter case, the effect could be driven by history of abuse or by other (hidden) group factors. We would like to point out that the correlation remained significant when history of maternal abuse was included as an independent covariate, suggesting that the effect is not solely driven by the factor abuse. In addition, one may argue that the scatter plots do not suggest primary group effects and that small group sizes may account for the absence of correlation in the within-group analyses. However, these considerations remain speculative and we cannot exclude other (hidden) group factors confounding the observed correlation. Thus, we have to acknowledge that a replication study in a larger sample is needed to prove a true dyadic linear relationship independent of group assignment.

Our findings in children replicate previous studies showing alterations of affect recognition in children with remitted depressed parents (Joormann & Gotlib, 2007; Lopez-Duran et al., 2013). Extending these findings, our present study is the first to show corresponding alterations between remitted mothers and their children. The negative processing bias in maternal affect recognition might influence the child's affect recognition abilities as the mother is usually the most important model from which the child learns emotional and social skills during the first years of childhood (Goodman & Gotlib, 1999). Children might have acquired a biased affect recognition through social learning in form of modeling processes. Children have been found to mirror negative cognitions of their depressed mothers, such as being more self-critical and having lower self-concepts (Downey & Coyne, 1990), and depressed mothers have been observed to frequently criticize their children (Webster-Stratton & Hammond, 1988). Our corresponding findings in children might reflect modeling of maternal negative thinking, or the experience of having been frequently reinforced to hold negative views about the world or oneself. Beside cognitive processes, one likely biological mediator might be the neuropeptide oxytocin which has been linked with affect recognition performance in healthy adults (Van Ijzendoorn & Bakermans-Kranenburg, 2012) and appears to be reduced in depressed mothers (Apter-Levy et al., 2014), as well as in individuals with history of childhood abuse (Heim et al., 2009).

Our data on remitted mothers suggest that children may be exposed to their mother's negative processing bias not only during acute depressive episodes but also during remission. This extended exposure might increase the risk that children likewise adopt this processing bias and may explain why we found such bias in the affected children, although their mothers were currently remitted. Although our correlational data do not prove a causal relationship between maternal and child alterations in

affect recognition, our parallel findings in mother-child dyads performing the identical task suggest transgenerational transmission of biased affect recognition.

This negative processing bias in children might place them at elevated risk for experiencing depressotypic feelings and thoughts similar to the ones exhibited by their mothers. This could make them more vulnerable to developing affective disorders themselves (Goodman et al., 2011).

4.3. The impact of additional maternal trauma

The present study distinguished two subgroups of remitted depressed mothers, namely mothers with and without a history of trauma (i.e., physical or sexual abuse). These two subgroups of mothers did not differ significantly in their affect recognition performance, nor did their children. This absence of a trauma effect is somewhat contrary to previous studies on affect recognition that have reported a fear and anger bias in individuals with a history of trauma (Dannlowski et al., 2012; Poljac et al., 2011; Rauch et al., 2000; Shin et al., 2005; van Harmelen et al., 2010). One explanation for this discrepancy might be that these previous studies have explicitly focused on the effects of trauma, thus studying individuals with trauma, but without depression. In contrast, the present study focused on effects of depression, thus studying individuals with history of both trauma and depression. It is possible that the effects of depression override effects of trauma in our study. Therefore, our data do not show isolating effects of trauma independent of depression. However, our data do permit the conclusion that the effect of depression reported here is not due to confounding effects of trauma. The effect of remitted depression on affect recognition exists independently of trauma, though replication of our results with larger sample sizes and a healthy control group with history of abuse is warranted.

5) Limitations

A number of limitations of the present study may be considered. First, it is acknowledged that the total number of children in each group was relatively small (control: n=14; depression only: n=14; depression & trauma: n=27) which is due to the challenge of recruiting mother-child dyads fulfilling all inclusion criteria. Second, our stimulus material consisted of (unfamiliar) adult faces only. In doing so, we relied on an established affect recognition task (Domes et al., 2008). It will be interesting to use child faces or a combination of child and adult faces in future studies. Further studies might also investigate the response of mothers to their own child's face, and the response of children to their own mother's face. Third, we acknowledge that we did not implement a statistical correction for multiple types of affect when testing for group effects. Because the ANOVAs for the interaction effect were significant, we conducted multiple post-hoc tests to explore which affect and group accounted for the initial effect. Furthermore, we had a priori hypotheses specifically for the recognition of sadness.

Fourth, we acknowledge that IQ scores differed numerically between children of healthy controls and children of remitted depressed mothers (108.1 versus 99.1, respectively). Although this difference did not reach statistical significance, probably due to small sample size and large variance in IQ scores, future studies with larger sample sizes should take differences in intellectual abilities into account. Fifth, the present data do not allow conclusions on the affect recognition abilities of our two patient groups prior to the onset of their depression. Longitudinal research in high-risk populations (Just et al, 2001) testing children and their never depressed mothers would be desirable to investigate transgenerational transmission of altered affect recognition in more detail.

6) Conclusions

Our findings may have clinical implications for both mothers and children. Even during remission, mothers with depression showed altered affect recognition, particularly concerning sad facial expressions. This persistent processing bias might contribute to the onset of future depressive episodes in the mothers and through social learning also impact on the offspring. Indeed, our cross-sectional and correlational data suggest that the bias is transmitted to the children. In the next generation, this bias may again increase the risk for developing depressive symptoms, as in the mothers. Our findings may therefore play a role in explaining the well established finding of increased behavioral and emotional problems in children of depressed parents (for a meta-analysis, see Goodman et al., 2011). Both mothers and children might benefit from early interventions focusing on social cognition with particular emphasis on affect recognition, involving also the modification of negative cognitions and strengthening parenting competencies.

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Conflict of interest

None.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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Table 1: Demographic and clinical data of study participants

	Control (N=21)		Depression (N=18)		Depression & Trauma (N=33)		
Mothers	M	SD	M	SD	M	SD	p
Maternal age in years	39.1	4.2	38.8	4.5	38.5	6.5	>.05
Maternal IQ	109.5	10.2	108.5	9.5	104.9	9.9	>.05
Maternal years of education	18.4	3.3	18.3	3.7	16.7	3.3	>.05
HAMD	1.6	1.4	2.5	2.4	2.6	1.9	>.05
	Control (N=14)		**Depression (N=14)**		**Depression & Trauma (N=27)**		
Children	M	SD	M	SD	M	SD	p
child age in years	8.4	2.2	8.4	2.1	7.7	1.6	>.05
child IQ	108.1	10.2	99.1	13.3	104.5	12.2	>.05
child sex (% girls)	50		50		67.8		>.05[a]

Notes: M: Mean; SD: standard deviation; HAMD: Hamilton Depression Scale; univariate analyses of variance (ANOVA) were performed; [a]chi-square calculation was performed

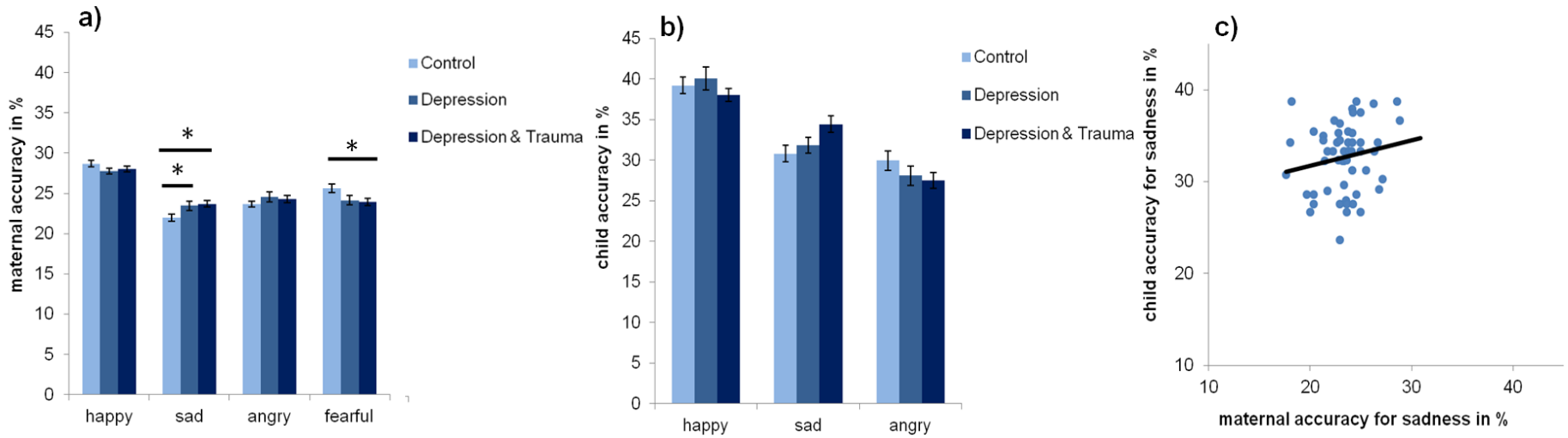

Figure 1: the accuracy score reflects the number of correct answers for a given affect category divided by the number of all correct answers; asterisks indicate significant post-hoc single comparisons (*p<.05, two-tailed); error bars represent standard errors in both directions; **a)** Maternal accuracy scores for control and both remitted depression groups. **b)** Child accuracy scores for control and both remitted depression groups. c) Significant dyadic correlation for accuracy for sadness across groups (r=.26, p=.045; two-tailed).

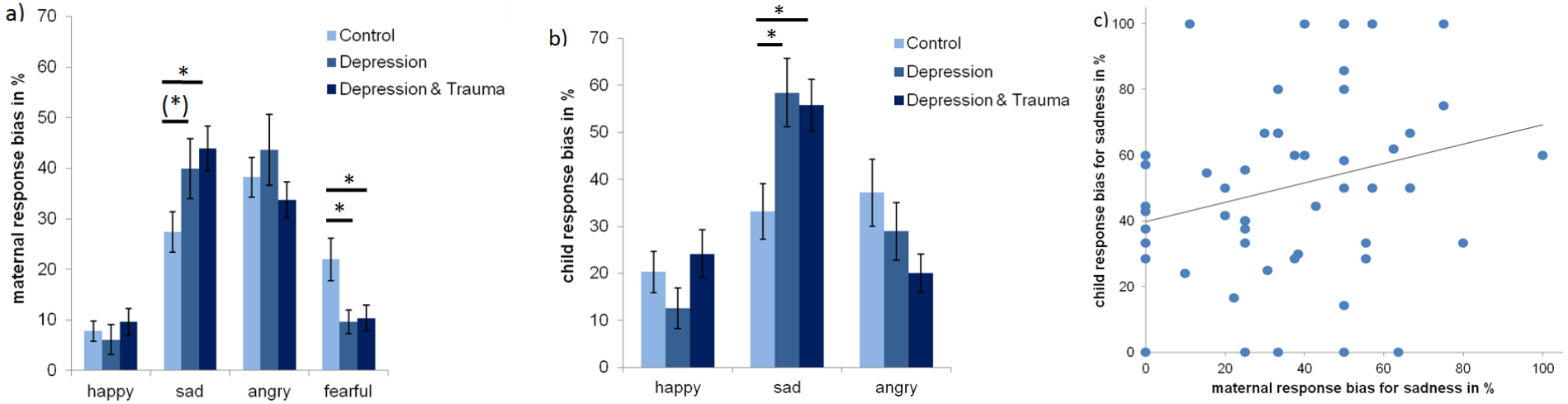

Figure 2: The response bias reflects the tendency to misinterpret facial expressions in favor of a certain affect category (happy, sad, angry, fearful); asterisks indicate significant post-hoc single comparisons (*p<.05 and (*)p<.10, two-tailed); error bars represent standard errors in both directions; **a)** Maternal response bias for control and both remitted depression groups. **b)** Child response bias for control and both remitted depression groups. **c)** At-trend level significant dyadic correlation for response bias for sadness across groups (r=.24, p=.066; two-tailed)

7.1.3 Study III

Title: Emotional availability in mother-child interaction: the effects of maternal depression in remission and additional history of childhood abuse

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Short title: maternal depression & emotional availability

All authors declare that they have no conflicts of interest related to this work and that they approve the final manuscript.

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Keywords: abuse, maltreatment, neglect; depression; maternal-child; child/adolescent; family/marital

Abstract

Background

The association between maternal depression and adverse outcomes in children is well established. Similar links have been found for maternal childhood abuse. One proposed pathway of risk transmission is reduced maternal emotional availability. Our aim was to investigate whether sensitive parenting is impaired in mothers with depression in remission, and whether among these mothers childhood abuse has an additional impact.

Methods

The mother-child interaction of 188 dyads was assessed during a play situation using the Emotional Availability Scales, which measure the overall affective quality of the interaction: maternal sensitivity, structuring, non-hostility, and non-intrusiveness. Mothers with depression in remission were compared to healthy mothers. Children were between five and 12 years old. Group differences and impact of additional childhood abuse were analyzed by one-factorial analyses of covariance and planned contrasts.

Results

Mothers with depression in remission showed less emotional availability during mother-child interaction compared to healthy control mothers. Specifically, they were less sensitive and, at trend-level, less structuring and more hostile. Among these mothers, we found an additional effect of severe maternal childhood abuse on maternal sensitivity: Mothers with depression in remission and a history of severe childhood abuse were less sensitive than remitted mothers without childhood abuse.

Conclusions

Our data suggest that depression impacts on maternal emotional availability during remission, which might represent a trait characteristic of depression. Mothers with depression in remission and additional severe childhood abuse were particularly affected. These findings may contribute to the understanding of children's vulnerability to develop a depressive disorder themselves.

1. Introduction

Having a depressed mother can have profound consequences for a child's emotional and behavioral well-being, such as developmental deficits, psychological problems, disruptive behavior and intellectual deficits.[1-5] Maternal history of childhood abuse has also been suggested as a risk factor for adverse development in children.[6,7] Furthermore, depression and childhood abuse often co-occur.[8] Pathways for the transmission of both maternal depression and history of childhood abuse have been proposed on different levels: genetic transmission, neurobiological alterations, observational learning of the child, as well as poor maternal parenting behavior.[9-12] Regarding parenting behavior, two issues remain to be elucidated: First, does maternal depression impact on parenting behavior during remission of depressive symptoms? Second, does a history of childhood abuse have an additional effect among these mothers? The present study sought to address these two questions.

1.1. Maternal depression and parenting

Symptoms of depression may prevent depressed mothers to have enough energy and capacity to respond to children's needs.[13,14] Leckman-Westin and colleagues demonstrated that depression contributed to child behavior problems only if mothers also showed poor parenting behavior.[15] Parenting behavior of depressed mothers is often characterized by less emotional availability,[16,17] which refers to the ability to share an emotionally healthy mother-child relationship.[18,19] Previous studies on emotional availability in acutely depressed mothers report reduced sensitivity,[20,21] less structuring,[22] increased hostility,[23] and intrusiveness.[24] While parenting behavior has well been studied during acute depressive episodes,[11] research on parenting behavior in mothers with remitted depression is scarce.[25-27] The present study will address this question in a first analysis step.

1.2. Maternal history of childhood abuse in the context of psychopathology

Patients often report additional history of childhood abuse, such as physical or sexual abuse.[28] Based on neurobiological[29,30] and treatment studies,[31,32] it has been suggested that depressed patients with and without childhood abuse represent two distinct subgroups of depression. This distinction may be critical for the investigation of maternal emotional availability, as childhood abuse has – independently of

depression - been associated with reduced parenting skills, [33,34]; but [35] such as less sensitivity,[36-41] less involvement,[42,43] and greater hostility and intrusiveness to the child. [44-46] An additional history of childhood abuse in mothers with remitted depression might pose a synergetic risk for dysfunctional parenting behavior. Only a few studies have investigated the impact of maternal childhood abuse on parenting in women with depression and suggest an additional effect.[47-49] To date, such studies relied on questionnaire data for parenting behavior, diagnostic status and childhood abuse. Additionally, it has been proposed that severity of childhood abuse is critical.[50] Therefore, in a second analysis step, we here studied mothers with remitted depression with different degrees of childhood abuse, i.e., with history of (1) no, (2) mild to moderate, and (3) severe childhood abuse.

We tested two hypotheses: (1) mothers with depression show reduced emotional availability toward their children during remission. (2) This effect is more pronounced in remitted mothers with additional history of childhood abuse (i.e. physical or sexual abuse), with stronger effects in mothers with more severe childhood abuse.

2. Methods

2.1. Participants & Procedure

The current study involved 188 mother-child dyads (N=99 healthy control mothers, N=89 mothers with remitted depression; see Table 1). Maternal groups did not differ with respect to their age, years of education, and IQ. Their children did not differ regarding their age, IQ and gender distribution between groups (see Table 1 for participants' characteristics). Healthy mothers were more likely to cohabit with the child's father than mothers with remitted depression (77% versus 42%, respectively).

Mother-child dyads were recruited in two German study sites (Berlin & Heidelberg) by advertisement (e.g., psychiatrists' and gynecologists' outpatients' clinics). Additionally, mothers from a previous study were re-contacted.[40,46] Healthy control mothers did not differ between study sites in age, years of education, partnership status and child's age and child's sex. As an inclusion criterion, mother and child had to live together, also in case of shared custody. Children were between five and 12 years of age and attended already primary school. All mothers were required to have a HAMD score of below or equal seven to assure full remission in case they had an episode of depression in the past.[52] Exclusion criteria for mothers were: neurological diseases, acute axis I disorders (i.e. anxiety disorders, post-traumatic stress disorder,

affective disorders, eating disorders, and alcohol or substance dependence) and lifetime history of schizophrenia or manic episodes as assessed by the Mini International Neuropsychiatric Interview (M.I.N.I.[53]), and one of the following three personality disorders: emotional-unstable, anxious-avoidant, antisocial personality disorder (based on the International Personality Disorder Examination (IPDE[54]). Mothers with depression in remission had the following comorbid life-time diagnoses: panic disorder (n=9), obsessive compulsive disorder (n=1), social phobia (n=2), post-traumatic stress disorder (n=2), generalized anxiety disorder (n=1), anorexia nervosa (n=2), and bulimia nervosa (n=2). Intake of benzodiazepines within the last six months was an exclusion criterion, because consumption and withdrawal of these substances may have particularly strong impact on mother-child interaction. Medication with antidepressants did not represent an exclusion criterion; however the dosage had to be stable for at least two weeks prior to study entrance.

To rule out differences in maternal intellectual abilities, we used a German vocabulary test (Wortschatztest, WST[55]). Exclusion criteria for children were: meeting DSM-IV criteria for autistic disorder and an IQ score below 70. To assess children's intellectual abilities we applied either the Culture Fair Intelligence Test I revised for children between five and eight years of age (CFT 1-R[56]) or the CFT 20-R[57] for children from the age of nine or above. Dropout was as follows: 36 mother-child dyads could not be re-contacted after they had agreed to participate. Eleven dyads were excluded because the mother was acutely depressed at testing time (n=6), met DSM-IV criteria for alcohol or drug dependence (n=2), or the child either met DSM-IV criteria for autistic disorder (n=2) or had an IQ score below 70 (n=1). Three dyads were not invited, because the child's father did not give informed consent for the child's study participation. We included 188 mother-child dyads in analysis.

Approval for the study was obtained by the ethics committees of the Charité – Universitätsmedizin Berlin and the Faculty of Medicine of Heidelberg. Written informed consent was obtained from all participants after the nature of the procedure was explained. The present study was performed within the framework of the UBICA ("Understanding and Breaking the Intergenerational Cycle of Abuse") multicenter project which investigates the effects of maternal history of abuse on mother-child interaction and child wellbeing.

2.2. Measures

Emotional Availability Scales (EAS, 4th Edition, Biringen, (2008)[51]): To observe maternal emotional availability mother-child dyads were videotaped in a standardized playroom setting. For the first 15 minutes, mother and child were told to play as they normally would in a free play situation. For further six minutes, dyads performed a puzzle task ("Shape by Shape") that was designed to be too difficult for the child. Mothers were instructed to help their child as they normally would do but not to solve the puzzle for the child. The EA scales are rated on a one to seven scale across the two situations. We were particularly interested in maternal emotional availability and will therefore report on the four adult scales.

In brief, high *maternal sensitivity* is characterized by positive and authentic maternal affect, maternal awareness of, and responsiveness to timing of child behavior. Low scores indicated maternal behavior that lacks general positive affect, appropriate awareness of, and responsiveness to child's emotional expressions. As sensitivity is meant to be a dyadic construct, a mother could only receive high scores if her child also appeared to be highly responsive and involving.[17] Maternal *structuring* addresses the ability to adequately scaffold a child's activities. *Non-intrusiveness* refers to a lack of over-protection, over-stimulation, and interference, therefore maintaining a child's autonomy. *Non-hostility* is described by lack of signs of anger, impatience, and boredom. Many studies have supported the validity of the EA scales with associations between emotional availability and mother-child attachment[20, 22] or maternal perspective taking. [21, 23] More detailed descriptions can be found in Biringen et al. (2014).[17]

EA scales were coded by three researchers (one senior clinical psychologist, and two psychologists who hold a Master's degree of clinical psychology), who have been approved as reliable to code by Zeynep Biringen after an extensive training period. Coders were blind to maternal history of depression and childhood abuse and videos were randomly assigned to them. Every video (n=188) was rated independently by at least two coders, coding discrepancies were resolved through discussion. For the maternal subscales, interrater reliability for pairs of raters ranged between r=.78 and r=.86 for "sensitivity", between r=.81 and r=.87 for "structuring", between r=.82 and r=.86 for "non-intrusiveness", and between r=.84 and r=.90 for "non-hostility"

(average-measure intra-class correlations), indicating excellent agreement.[58] The internal consistency coefficient for the four adult scales was Cronbach's α=.81, indicating excellent internal reliability of the construct of maternal emotional availability.[58]

Maternal depression: To assess maternal history of depression (and other diagnoses of acute and lifetime DSM-IV axis I disorders), we implemented the Mini International Neuropsychiatric Interview (M.I.N.I.[53]), a fully structured diagnostic interview for screening DSM axis I disorders. Previous research has shown good inter-rater reliability.[59,60] To assure full remission, we additionally applied the Hamilton Depression Scale (HAMD[61,62]). A score of below or equal seven is considered as remission.[63] The HAMD has good concurrent validity with other depression severity assessment scales.[64]

Maternal history of childhood abuse: As questionnaire data on childhood abuse may not capture the relevant context and may be limited in encompassing breadth and timing of experience, we conducted the Childhood Experience of Care and Abuse interview (CECA[65]; German version[66]). This is a semi-structured clinical interview that is designed to collect retrospective accounts of adverse childhood experience (up to an age of 17 years), such as physical and sexual abuse, emotional abuse, neglect, and antipathy. All experiences were rated by the interviewer on 4-point scales of severity ('severe, 'moderate', 'mild' or 'little/none') according to predetermined criteria and manualized threshold examples. Interviewers had been intensively trained by the developer of the interview. Good interrater reliability has been demonstrated for the CECA[65,67]. The physical and sexual abuse scales were used to denote history of childhood abuse for our analyses.

2.3. Statistical Analysis

To examine possibly confounding group differences, we first explored descriptive data on maternal and child demographic and clinical characteristics. To test our first hypothesis, we used univariate analyses of covariance (ANCOVA) with history of depression (yes/no) as between-subject factor and partnership status, and HAMD scores as covariates. As it has been suggested to account for additional adverse childhood experiences,[38] we also took the sum score of the CECA main scales (physical abuse, sexual abuse, neglect, antipathy, emotional abuse) as covariate. Bonferroni correction was applied to account for multiple testing ($p \leq .0125$).

In a second analysis step, ANCOVAs were run to evaluate effects of additional history of childhood abuse on emotional availability among the remitted group compared to a healthy control group without any history of childhood abuse (i.e. a score of 'little/none' on both CECA scales physical and sexual abuse; n=56). We subdivided the remitted depression group according to their degree of childhood abuse in three groups: remitted depression a) without history of childhood abuse (i.e. a score of 'little/none' on both CECA scales physical and sexual abuse; n=19), b) with mild to moderate history of childhood abuse (i.e. a score of 'mild' or 'moderate' on one or both CECA scales physical and sexual abuse; n=56), c) with severe history of childhood abuse (i.e. a score of 'severe' on one or both CECA scales physical and sexual abuse; n=14). We added partnership status, HAMD scores, as well as the remaining CECA main scales (neglect, antipathy, emotional abuse) as covariates. Bonferroni correction was applied to account for multiple testing ($p \leq .0125$). As we were particularly interested in the comparison of mothers with remitted depression with and without childhood abuse, we chose the remitted group without childhood abuse as reference group for post-hoc contrast analyses. If the contrast analysis revealed a significant result, we further confirmed our hypothesis by a hierarchical regression analysis within mothers with remitted depression. HAMD scores, as well as the remaining CECA main scales (neglect, antipathy, emotional abuse) were entered as one block in the first step. In the second step, a sum score of physical and sexual childhood abusive experiences was entered with lower scores indicating higher severity of childhood abuse. All calculations were conducted using SPSS for Windows (Version 18).

3. Results

Impact of remitted depression on maternal emotional availability

Sensitivity: We found a significant effect of remitted depression on maternal sensitivity scores ($F_{(1,181)}=10.034$; $p=.002$; $\eta^2=.052$). Remitted mothers had significantly lower sensitivity scores than healthy mothers (Table 2). Assessing the effect of partnership status, we found no significant influence on maternal sensitivity ($F(1,181)=1.843$; $p=.176$; $\eta^2=.010$). In addition, we used a one-stage random sample

design to stratify our sample by the presence of the father, and found the same effect of depression in remission (Wald-F(1,87)=22.767, p=.000).

Structuring: The effect of remitted depression showed a trend toward significance ($F_{(1,181)}$=5.236; p=.023; η^2=.028). Remitted mothers tended to scaffold the activity of their child to a lesser extent than healthy controls.

Intrusiveness: There was no significant effect of remitted depression on maternal intrusiveness ($F_{(1,181)}$=0.444; p=.51; η^2=.002).

Hostility: We found a trend-wise effect of remitted depression on hostility ($F_{(1,181)}$=3.928; p=.038; η^2=.024). Remitted mothers tended to show more signs of hostility than healthy controls.

Impact of additional history of childhood abuse on emotional availability

To test the additional impact of maternal childhood abuse, we computed a one-factorial ANCOVA consisting of four groups of mothers: (1) healthy without childhood abuse, remitted depression (2) without childhood abuse, (3) with mild to moderate childhood abuse, and (4) with severe childhood abuse.

Sensitivity: We found a significant effect of group ($F_{(1,135)}$=6.689; p<.001; η^2=.129). Planned contrasts revealed that remitted mothers with severe childhood abuse showed significantly lower sensitivity compared to remitted mothers without childhood abuse (p<.01; Figure 1, Table 3). There was no difference between remitted mothers without childhood abuse and remitted mothers with mild to moderate degrees of childhood abuse (p>.05). Remitted mothers without childhood abuse had lower sensitivity scores than healthy control mothers without childhood abuse (p<.05).

Regression analysis revealed that the sum score of physical and sexual childhood abuse tended to be a significant predictor (beta=.253; p=.071) for maternal sensitivity, explaining 6.4% of the variance. Regression results are displayed in Table 4.

Structuring: There was a trend for the effect of group ($F_{(1,135)}$=2.885; p=.038; η^2=.06). Planned contrasts were not analyzed.

Intrusiveness: The main effect of group did not reach significance ($F_{(1,135)}$=2.225; p>.05; η^2=.05). Planned contrasts were not analyzed.

Hostility: We found a significant main effect of group ($F_{(1,135)}$=3.877; p=.011; η^2=.08). Planned contrasts revealed that there was no significant difference between remitted mothers with severe childhood abuse and remitted mothers without childhood abuse (p=.088). There were no significant differences between remitted mothers without childhood abuse and remitted mothers with mild to moderate childhood abuse (p>.05). Remitted mothers without childhood abuse showed more signs of hostility than healthy control mothers without childhood abuse (p=.051).

4. Discussion

In this present study, parenting behavior has been observed in 188 mother-child dyads to investigate the effect of remitted depression and of additional childhood abuse on maternal emotional availability. We found impaired maternal sensitivity, and trend-wise reduced structuring and non-hostility in remitted mothers. Within this group of remitted mothers, the sub-group with history of severe childhood abuse showed significantly lower sensitivity compared to the sub-group without childhood abuse. Our findings suggest that (a) depression impacts on maternal emotional availability also during remission and (b) the sub-group of mothers with additional history of severe childhood abuse seems to be particularly affected.

4.1. *Impact of maternal history of depression on maternal emotional availability*

Previous studies on maternal parenting in acutely depressed mothers have reported reduced emotional availability.[11,20-24] Adding to this literature, we here found similar alterations of maternal sensitivity, structuring abilities, and maternal hostility in mothers remitted from depression. These data suggest that children of mothers suffering from depression may be affected by impaired maternal parenting behavior not only during the mothers' acute depressive episodes but also during remission. It is obvious that persistent alterations of parenting behavior will have greater impact on the children's development and well-being, e.g., it may affect the child's intellectual development[68,69] and add to emotional and behavioral problems[5, 70-72]

While the majority of studies on maternal parenting in depression have focused on acute depressive episodes, a few earlier studies have investigated remitted mothers.[25-27] One study examined the speech pattern of mothers with remitted

depression and found them to respond less quickly to their 3-year-old infants.[25] Stein and colleagues observed mother-infant interactions and found remitted mothers to less maintain their infant's interest and attention in playing.[26] In the last study, mother-adolescent dyads were asked to reflect on their relationship,[27] and remitted mothers were reported to be less engaged with their adolescent child. The present study differs from previous studies on remitted mothers in the following aspects: 1) To the best of our knowledge, this is the first study investigating the parenting behavior of remitted mothers of school-aged children (five to 12 years old). This age range might be an important time window for the impact of remitted depression on children's intellectual achievements and social adjustment.[73] 2) We used the Emotional Availability Scales,[50] which have the advantage of being an emotion-focused measure that refers to the overall affective quality of the relationship and is assessed by independent raters. Furthermore the scales take a dyadic perspective into account where the child is not only the recipient but also contributes to the interaction. We acknowledge that the scoring of maternal emotional availability might also depend on the child's behavior and reactions which we have not analyzed in the present study. Future studies may address the impact of the child's behavior and temperament on maternal parenting behavior.

The question arises why mothers with depression exhibit impaired parenting behavior even during remission. One likely explanation is that the impairments are direct consequences of the depression, representing alterations that persist even after remission of typical depressive symptoms. The impairments reported here may thus represent a trait characteristic of depression. This explanation is supported by a growing number of studies in remitted patients showing persisting impairments also in other cognitive and affective domains.[74,75] We acknowledge that we do not have data on maternal emotional availability prior or during acute depressive episodes which would be necessary to definitely confirm this assumption. However, our results in remission may motivate mothers at all states of depression to actively seek treatment of both depression and impaired maternal sensitivity. Time of remission might be a critical period for mothers to train and improve their parenting qualities. An alternative explanation is that residual depressive symptoms in our remitted mothers drive the effects. Although HAMD scores differed significantly between groups, we consider this explanation very unlikely, given that the mean HAMD score of 2.5 in the remitted depression group is by no means clinically relevant. In addition, HAMD

scores were included as covariates in our analyses. A third explanation would be that impaired parenting behavior is related to secondary (potentially hidden) group factors. To exclude such confounding factors we have matched groups for mothers' and children's age and sex, and included partnership status as a covariate (which turned out to have no significant effect on maternal sensitivity). In an additional analysis, we stratified our groups by maternal partnership status; this analysis still showed a significant effect of remitted depression on maternal sensitivity. We acknowledge that further confounding factors (e.g., supportiveness of child's father, other social support, impact of additional life events) may exist that were not considered in our study.

Given the high incidence of childhood abuse in depression[76] and the impact of maternal childhood abuse on parental behavior,[33,34] history of childhood abuse must be considered a particularly important factor in any study investigating the effect of depression on parenting behavior. To account for this factor we have taken the following steps: in analysis 1, comparing mothers with versus without history of depression, we have included history of childhood abuse as a covariate. In analysis 2, distinguishing sub-groups of depression, we provide a direct comparison between remitted mothers without childhood abuse and healthy control mothers without childhood abuse. We thus conclude that the reported effect of remitted depression exists independent of effects of childhood abuse.

4.2. *Impact of severity of childhood abuse on emotional availability among mothers with depression in remission*

Several studies showed that a considerable number of individuals with depression also have a history of childhood abuse.[76,77] In theory, effects of remitted depression and childhood abuse could add up. Alternatively, it is also possible that the effect of maternal psychopathology is more pronounced and overrides the effect of childhood abuse. Our data show, besides the effect of remitted depression, an additional effect of severe childhood abuse on maternal emotional availability. Specifically, remitted mothers with a history of severe childhood abuse showed reduced maternal sensitivity during mother-child interaction. Our regression analysis confirmed the

additional effect of severity of childhood abuse among mothers with depression in remission, however only at trend-level.

Our data show, besides the effect of remitted depression, and additional effect of physical and sexual childhood abuse on maternal emotional availability. Specifically, severity of childhood abuse predicted reduced scores for maternal sensitivity even after controlling for history of depression.

Although several studies have investigated the effects of childhood abuse[33,34,40] and some studies the effects of remitted depression,[25-27] only few studies have investigated both risk factors at the same time.[47-49] These studies differ from the present study in the following regards: first, previous studies nicely disentangled effects of childhood abuse and depression, but did not specifically focus on additive effects. Second, previous studies also included acutely depressed mothers, while the present study only included remitted mothers. Third, in comparison to previous studies, we directly observed mother-child interaction during a play situation and assessed its quality by independent and blinded raters using the EA scales. This allowed us to observe and rate more subtle affective and behavioral aspects of maternal parenting behavior that are presumably not captured by self reports based on questionnaire measures.

Notably, the additional effect of childhood abuse was only found in remitted mothers with severe childhood abuse. Severe abuse was in our present study defined as severe physical maltreatment (e.g., ongoing physical abuse in childhood with life threatening or severe injuries) or severe sexual abuse (e.g., repeated sexual contact with a relative or known adult). Remitted mothers with mild to moderate childhood physical or sexual abuse (e.g., including being repeatedly slapped or hit by a belt, or one's breasts and genitals being touched) did not differ significantly from remitted mothers without childhood abuse. The absence of an additional effect of mild to moderate childhood abuse might be due to sample size. An alternative explanation is that, in these cases, the history of depression may be the determining factor, overriding effects of mild to moderate childhood abuse.

Notably, the additional effect of childhood abuse was only found for maternal sensitivity. One explanation might be that physical and sexual childhood abuse specifically impacts on maternal sensitive behavior. An alternative explanation is that,

for the other subscales, the history of depression may be the determining factor, overriding effects of physical and sexual childhood abuse.

5. Limitations

A number of limitations of the present study have to be considered. First, our total sample size (n=188) and especially the one of the remitted group with severe experiences of childhood abuse were fairly small (n=14), which is due to the challenge of recruiting mother-child dyads fulfilling all inclusion criteria. Second, the present data do not allow conclusions on maternal parenting behavior during and prior to the onset of maternal depression. An acutely depressed comparison group or longitudinal investigations of maternal sensitivity would be desirable to disentangle preexisting alterations from consequences of depression. Third, other types of childhood abuse, such as emotional abuse or neglect, could also have adverse effects on the mother-child interaction [78]. The effects of these types of abuse were not studied here, because maternal childhood abusive experiences were defined as physical or sexual abuse in the present study. Accordingly, our recruitment did not focus on emotional abuse and neglect and sample sizes are rather unbalanced with regard to these variables (neglect: severe (n=5), moderate (n=10), mild (n=38), little/none (n=92); emotional abuse: severe (n=5), moderate (n=5), mild (n=17), little/none (n=118); however, in our analyses, we took these forms of childhood abuse as covariates into account. Fourth, because the present study focused on mothers with depression, it does not provide the comparison between healthy mothers with versus without history of childhood abuse. This comparison would have allowed replicating earlier studies that have identified the effect of childhood abuse (that exists independent of depression) and disentangled effects of childhood abuse and depression.[47; 49] Fifth, the age range of children has been relatively wide for studying mother-child interaction. However, it should be noted that there was no difference in children's age between groups. Sixth, we acknowledge that only the results for maternal sensitivity remained significant after Bonferroni correction.

6. Conclusion

Altogether, during remission, mothers with depression showed reduced emotional availability, particularly maternal sensitivity. This finding appears to be relevant for both mothers and children, as persistently reduced sensitivity may contribute to continuing social interaction problems in mothers and through social learning also impact on the offspring. Our findings can therefore help to explain the well-established unfortunate finding of increased behavioral and emotional problems in children of parents with depression. Clinicians should be aware that maternal sensitivity might be reduced even though mothers have remitted from typical symptoms of depression. Our results in remission may motivate mothers to actively seek treatment both of depression and of impaired maternal sensitivity. For affected mothers, the remission status might be a critical time period to train and improve their parenting qualities. In addition, our results in remitted mothers suggest an additional effect of severe childhood abuse. Both mothers and children might benefit from early interventions focusing on parenting behavior with particular emphasis on maternal sensitivity.

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Table 1: Participants' demographic and clinical characteristics

	Healthy control mothers (N=99)	Mothers with depression in remission (N=89)	p
Mothers			
Age (SD)	39.2 (5.2)	40.2 (6.0)	>.05
Years of education (SD)	17.4 (3.3)	16.9 (3.8)	>.05
IQ (SD)	106.1 (11.4)	106.3 (11.2)	>.05
Living together with child's father (% yes)	76.8	41.6	<.001[a]
HAMD (SD)	1.2 (1.5)	2.5 (2.1)	<.001[b]
Number of depressive episodes (SD)	---	2.3 (1.5)	
Mean time elapsed since last depressive episode (months (SD))	---	61.6 (58.6)	
Children			
Age	7.8 (1.5)	8.3 (1.7)	>.05
IQ	107.1 (12.7)	104.5 (13.5)	>.05
Sex (% girls)	51.5	61.8	>.05

Notes: SD: standard deviation; [a]chi-square calculation; [b]t-test two-sided;

Table 2: Means and Standard Deviations of Emotional Availability Scales in mothers

	Group		
	Healthy control mothers (n=98)	**Mothers with depression in remission (n=89)**	**P**
Sensitivity (SD)	4.6 (0.9)	4.0 (0.9)	<.01[a]
Structuring (SD)	4.8 (0.8)	4.4 (0.8)	<.05
Non-Intrusiveness (SD)	5.2 (0.9)	5.1 (1.1)	.78
Non-Hostility (SD)	5.8 (1.0)	5.4 (1.1)	<.05

Notes: SD: standard deviation; [a]statistically significant after Bonferroni correction for multiple testing was applied (significance threshold: p<.0125)

Table 3: Means and Standard Deviation of Emotional Availability Scales in mothers: effect of additional history of childhood abuse

	Group				
	HC w/o CA (n=56)	**rMDD w/o CA (n=19)**	**rMDD & mild-moderate CA (n=56)**	**rMDD & severe CA (n=14)**	**p[a]**
Sensitivity (SD)	4.7 (0.8)	4.2 (0.9)[c,d]	4.0 (0.9)	3.6 (1.2)	<.001[b]
Structuring (SD)	4.1 (0.8)	4.4 (0.8)	4.5 (0.7)	4.1 (0.8)	<.05
Non-Intrusiveness (SD)	5.3 (0.8)	5.2 (1.1)	5.3 (1.0)	4.6 (1.3)	.09
Non-Hostility (SD)	6.0 (0.9)	5.5 (1.1)	5.5 (1.0)	5.0 (1.2)	<.05

Notes: HC: healthy controls; rMDD: mothers with at least one remitted episode of depression; CA: childhood abuse; w/o: without; SD: standard deviation; mild-moderate CA is defined by a score of 'mild' or 'moderate' on the physical or sexual subscale of the Childhood Experience of Care and Abuse (CECA) Interview; severe CA is defined by a score of 'severe' on the physical or sexual subscales of the CECA Interview; [a]p-values indicate significance level of the main effect of group (ANCOVA);[b]statistically significant after Bonferroni correction for multiple testing was applied (significance threshold: p<.0125); [c]planned contrast between HC and rMDD without CA significant at p<.05; [d]planned contrast between rMDD without any CA and rMDD with severe CA significant at p<.05

Table 4: Hierarchical regression analysis predicting maternal sensitivity from demographics, and severity of childhood abuse among mothers with depression in remission (n=89)

Emotional availability Scale	Predictor Variables	R2 Change	R	R2 adjusted	F	beta coefficient (95% CI)	p
Sensitivity	Step 1	.026	.161	-.020	0.561		>.05
	HAMD					-.078 (-.135 - .063)	
	Neglect					-.140 (-.418 - .110)	
	Antipathy					-.004 (-.229 - .222)	
	Emotional Abuse					.088 (-.173 - .372)	
	Step 2	.038	.253	.007	1.133		>.05
	Childhood abuse					.253 (-.013 - .329)	0.071

Notes: HAMD: Hamilton Depression Scale (Hamilton, 1970); Childhood abuse: sum score of physical and sexual childhood abuse

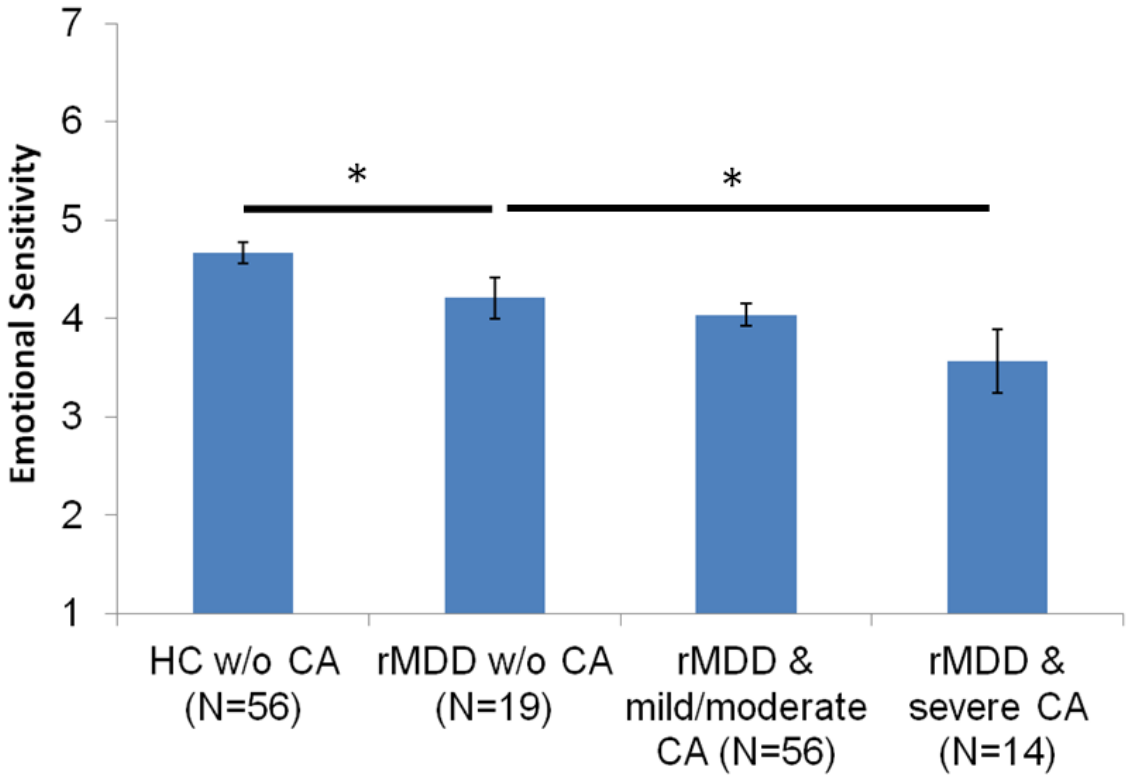

Figure 1: HC: Healthy control mothers; rMDD: mothers with at least one remitted episode of depression; w/o: without; CA: childhood abuse; mild-moderate CA is defined by a score of mild or moderate on the physical or sexual subscale of the Childhood Experience of Care and Abuse (CECA) Interview; severe CA is defined by a score of severe on the physical or sexual subscales of the CECA Interview; asterisks indicate planned contrast between 'HC w/o CA' and 'rMDD without any CA' (p=.039) and between 'rMDD without any CA' and 'rMDD with severe CA' (p=.009)

7.2 Contributions to conferences

Wissenschaftliche Vorträge

Kluczniok, D., Fuchs, A., Führer, D., Zietlow, A.L., Hindi Attar, C., Dittrich, K., Reck, C., Winter, S., Moehler, E., Heinz, A., Herpertz, S.C., Brunner, R., Boedeker, K., Bermpohl, F. 2015. Hormonelle Veränderungen bei Mutter-Kind Dyaden: die Rolle von mütterlicher Kindheitsmisshandlung**.** DGPPN-Kongress, Berlin.

Kluczniok, D., Fuchs, A., Führer, D., Zietlow, A.L., Hindi Attar, C., Dittrich, K., Reck, C., Winter, S., Moehler, E., Heinz, A., Herpertz, S.C., Brunner, R., Boedeker, K., Bermpohl, F. 2015. From generation to generation: effects of maternal history of childhood maltreatment and depression on mother-child interaction. 4th German health research meeting on behavioural disorders related to violence, Berlin.

Kluczniok, D., Führer, D., Hindi-Attar, C., Bödecker, K., Lehmkuhl, U., Heinz, A., Bermpohl, F., 2013. Affekterkennung bei Mutter-Kind-Dyaden: Die Rolle von Trauma und Depression, 2nd German health research meeting on behavioural disorders related to violence, negelect, maltreatment, and abuse in childhood and adolescence – UBICA, Hamburg.

Posterpräsentation:

Kluczniok, D., Hindi Attar, C., Brunner, R., Herpertz, S., Fydrich, T., Boedeker, K., Bermpohl, F., 2015. Transgenerationale Effekte von mütterlicher Depression auf die kindliche Affekterkennung. DGKJP-Kongress, München.

Kluczniok, D., Hindi Attar, C., Führer, D., Bierbaum, A.-L., Jaite, C., Roth, M., Boegen, I., Röpke, S., Heim, C., Bödeker, K., Lehmkuhl, U., Bermpohl, F., 2014. Transmission of traumatic childhood experiences across generations: mother-child interaction in mothers with borderline personality disorder. ESSPD-Kongress, Rom.

Kluczniok, D., Führer, D., Hindi Attar, C., Herpertz, S., Brunner, R. Bödeker, K, Bermpohl, F., 2014. How are children's hormonal reactions influenced by maternal trauma and depression: the role of maternal sensitivity. DeGPT Kongress, Hamburg.

Kluczniok, D., Neubecker, J., Piepka, F., Poppinga, S., Heim, C., Herpertz, S., Brunner, R., & Bermpohl, F., 2013. How does maternal sensitivity influence stress and bonding reactions in their child? DGPPN-Kongress, Berlin.

Kluczniok, D. & Cooper, Z., 2012. Assessing therapist competence: Development of a knowledge test of enhanced CBT for eating disorders, 27. DGVT Kongress für Klinische Psychologie, Psychotherapie und Beratung, Berlin.

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Eidesstattliche Erklärung

Hiermit erkläre ich an Eides statt,

- dass ich die vorliegende Dissertation selbstständig und ohne unerlaubte Hilfe verfasst habe,
- dass ich die vorliegende Dissertation an keiner anderen Universität oder wissenschaftlichen Einrichtung eingereicht habe und keinen Doktorgrad in dem Fach Psychologie besitze.
- dass mir die Promotionsordnung Nr. 34/2006 der Mathematisch-Naturwissenschaftlichen Fakultät II vom 17.01.2005, geändert am 03. August 2006, bekannt ist.

Berlin, den 15.01.2016

Dorothea Kluczniok